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OBSERVATIONS ON INFANTILE TETANY*

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In an article entitled "Observations on the Calcium Content of the Blood in Infantile Tetany and the Effect of Treatment by Calcium" Howland and Marriott [1] reviewed the essential points in the development of our knowledge of the disease, discussed the theories of its causation, the rôle of calcium and phosphates in its pathogenesis and the relationship between this condition and rickets. They determined the calcium content of the serum in a large series of cases of active tetany, and studied the effect of the administration of calcium chlorid on the clinical manifestations of the disease and on the calcium content of the serum. They concluded as follows:

> In tetany during the active symptoms the calcium of the serum is invariably greatly reduced and may fall as low as 3.5 mg. The average calcium content of the serum in eighteen cases was 5.6 mg. In convulsive disorders other than tetany there is no reduction in the calcium of the serum.....Cathodal hyperexcitability has invariably been accompanied by a marked reduction of the calcium of the serum. Calcium administration produces a prompt effect upon the course of tetany. In a few hours the spasmodic symptoms disappear. The calcium must, however, be continued for a long time. Calcium chlorid administered by mouth causes an increase in the calcium of the serum coincident with the cessation of symptoms, although in most instances the calcium of the serum does not return to quite normal figures.

In the last three years several papers have appeared on tetany or allied conditions in which are found determinations of calcium in the blood or serum that would seem to throw some doubt on the importance of the low calcium content, which is found in tetany, or on the close connection between the calcium content of the serum and the presence of manifestations of tetany. It is our purpose to discuss these papers at a future time when we wish to consider the sources of error in calcium determinations. In this paper we desire to present (1) observations in confirmation of the previous work of Howland and Marriott, (2) further observations on the concentration of inorganic phosphorus in the serum of patients, the subjects of active tetany, (3) the relationship between the sum of the univalent cations, sodium and potassium,

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* From The Harriet Lane Home, The Johns Hopkins Hospital, and the Department of Pediatrics, The Johns Hopkins University.

1. Howland, J., and Marriott, W. McK.: Quart. J. Med. **11**:289, 1918.

and the divalent cations calcium and magnesium. The method of procedure was essentially the same as that described in the previous paper. A number of methods were used for the determinations of calcium in the serum. These and the methods used to determine sodium, potassium and magnesium in the serum have been described elsewhere.[2]

Because of the fact that the determinations of all the inorganic constituents requires more blood than it may be advisable to obtain from a small infant, we have in some instances determined only the calcium, magnesium and inorganic phosphorus, in others only the sodium and potassium. In a few cases determinations of all of the inorganic constituents have been made from the same sample.

When symptoms of active tetany have been present (carpopedal spasm, laryngismus, convulsions), we have regularly found the calcium of the serum much diminished and the irritability of the nerves to the galvanic current greatly increased. It is true that the electrical reactions vary considerably from day to day and even from hour to hour, but with evidences of active tetany it is the nearly invariable rule to find COC or CCT $<$ 5 ma. and AOC $<$ ACC and the calcium concentration of the serum less than 7.5 mg. (often less than 5 mg.) per hundred c.c. When the evidences of tetany are not active COC may be greater than 5 ma., but if the calcium is less than 8.5 mg. per hundred c.c., which is usually the case, the anodal reversal almost always remains. Calcium chlorid by mouth, frequently repeated, will abolish the evidences of active tetany and will increase the calcium concentration of the serum to nearly or quite normal figures. With increasing experience we are inclined to give rather larger quantites of calcium chlorid, i. e., from 10 to 15 grains instead of 7½ grains every four hours. The action is rather more prompt and the calcium level that is reached somewhat higher when larger doses are given.

The observations of Binger,[3] that convulsions may be produced in dogs by the intravenous injection of alkaline phosphate, led Howland and Marriott[1] to determine the inorganic phosphate of the serum in four cases of active tetany in order to see whether the low calcium could be referred to a high orthophosphate serum content. They found 1, 3, 4 and 2.7 mg., respectively, of inorganic phosphorus. These figures, in the absence of many determinations on normal infants, were considered to be within normal limits. In the last two years Howland and Kramer[4] have determined the inorganic phosphate of the serum

2. Kramer, B., and Howland, J.: J. Biol. Chem. **43**:35, 1920; Kramer, B., and Tisdall, F. F.: Bull. Johns Hopkins Hosp. **32**:44, 1921; J. Biol. Chem. **46**:339, 467, 1921; Marriott, W. McK. and Haessler, F. H.: J. Biol. Chem. **32**:233, 1917.

3. Binger, C.: J. Pharmacol. & Exper. Therap. **10**:105, 1917.

4. Howland, J., and Kramer, B.: Am. J. Dis. Child. **22**:105 (Aug.) 1921.

in a large series of normal children. They found the concentration to average 5.4 mg. per hundred c.c. with a minimum of 4 mg. and a maximum of 7.1 mg., the higher values being usually found in the serum of exclusively breast fed children.[5] With this in mind we have determined the inorganic phosphorus of the serum with a number of children with tetany. The results are given in Table 1.

This table shows that in about half the cases the phosphorus concentration is within normal limits or slightly above the normal. This is in marked contrast with cases of uncomplicated rickets, i. e., without tetany, in which we have found a much reduced inorganic phosphate serum content.

Iversen and Lenstrup[7] have recently reported determinations of acid soluble and acid insoluble phosphorus in whole blood and plasma

TABLE 1.—CALCIUM AND INORGANIC PHOSPHORUS IN SERUM OF PATIENTS WITH TETANY NOT RECEIVING COD LIVER OIL

	Age	Date	Ca, Mg. per 100 C.c.	P, Mg. per 100 C.c.	
G. C. (colored)	7 mos.	2/17/21	5.7	4.4	
		2/23/21	10.4	...	After treatment with $CaCl_2$
W. B. (colored)	6 mos.	12/24/20	5.4	5.4	
L. B. (white)	5 mos.	11/22/20	6.2	4.4	
J. T. (colored)	11 mos.	2/16/21	7.0	7.0	
E. H. (colored)	3 mos. (premature)	1/21/21	7.8	5.8	No active symptoms; from electrical reactions and low Ca content of serum evidently latent tetany
J. J. (colored)	5 mos.	11/18/20	7.8	3.0	
G. J. (colored)	13 mos.	1/ 8/21	6.6	3.6	
		1/12/21	8.3	...	After treatment with $CaCl_2$
		2/ 4/21	10.0	4.4	
J. L. (white)	6 mos.	10/23/20	5.6		
		10/29/20	7.7	0.6	After treatment with $CaCl_2$
		11/18/20	8.5	2.4	

with a series of four cases of tetany. The acid soluble phosphorus in the plasma was found to vary from 2.9 to 5.0 mg. per hundred c.c. of plasma.

Although Jeppson and Klercker[8] produced electrical excitability in both animals and children by feeding large amounts of alkaline potas-

5. McKellips, De Young and Bloor,[6] recently reported findings regarding the inorganic phosphorus content of the plasma of twenty-three newly born infants. They found an average of 3.0 mg. for boys and 3.4 mg. for girls in 100 c.c. Most of the infants were losing weight when the samples of plasma were obtained. They could not, therefore, be regarded as normal. The diet of the infants is not mentioned. We have no figures of our own for infants so young as these. For older infants our observations on normal infants have been so numerous and so consistent that we are compelled to consider the figures that we report above as the average for normal infants. Our views are supported by the findings of Iverson and Lenstrup.

6. J. Biol. Chem. **47**:53, 1921.

7. Iversen, P., and Lenstrup, E.: Forh. ved Første Nordiske Kongres for Paediatri, 79, 1920.

8. Jeppson, K., and Klercker, O.: Ztschr. f. Kinderh. **28**:71, 1921.

sium phosphate, and emphasize the large phosphate content of the food of many infants with tetany, it would be hazardous to venture an explanation for tetany in the light of our studies which show a marked irregularity in the phosphorus concentration of the plasma or serum. It is evident that the amount of phosphorus that we have determined is not sufficient to account for the calcium diminution.

The Ratio of Monovalent to Divalent Cations in Serum of Patients with Tetany.—The work of Biedermann,[9] Loeb,[10] Matthews,[11] Mines[12] and Keith-Lucas[13] has emphasized the importance of the inorganic constituents of the blood serum. In a number of studies the necessity for a proper balance between sodium and potassium, on the one hand, and calcium and magnesium, on the other, for the maintenance of a proper irritability of muscle and nerve has been shown. Many writers on tetany for the last ten or fifteen years have speculated on the relationship between the concentration of sodium and potassium and of calcium and magnesium. With no accurate methods for the determination of sodium and potassium in the serum, no proof of an altered relationship in the serum could be adduced. In order to determine whether there is an abnormal ratio in the serum between sodium and potassium, calcium and magnesium methods have been worked out in this laboratory during the last three years which enable the sodium and potassium to be determined with a high degree of accuracy in the fresh serum or in ashed serum. Making use of these methods we have determined these inorganic constituents of the serum on a series of normal infants and on a number with active tetany.

In Table 2 are given the results of the determinations of sodium and potassium and calcium on the serum of five children with active tetany.

In a large series of cases of active tetany we have found the average calcium content of the serum to be about 5.4 mg., or, roughly, half the normal. In ten cases of active tetany we have found the average sodium concentration to be 325 mg., which is practically normal. The highest concentration was 337 mg. and the lowest 320 mg. In a similar number of cases of active tetany we have found the average potassium concentration of the serum to be 24.3 mg., which is about 25 per cent. above the normal average of 19.5 mg. The highest concentration was 28.4 mg. and the lowest 19.0 mg. In ten cases of active tetany we have found the magnesium concentration to be 1.9 mg., the average with normal infants being about 2.5 mg. The highest concentration was

9. Biedermann: Sitzungsberichte der Wiener Akademie der Wissenschaften, **82**: Pt. 3, 1880.

10. Loeb, J.: Beitr. z. Physiol. Festschrift für Adolf Fick, 1899. Loeb, J.: Arch. f. d. ges. Physiol. **91**:248, 1902.

11. Matthews, A. P.: Am. J. Physiol. **11**:455, 1904.

12. Mines, G. R.: J. Physiol. **37**:408, 1908.

13. Keith-Lucas: J. Physiol. **37**:459, 1908.

2.9 mg. and the lowest 1.1 mg. It is obvious from these figures and those contained in Table 2 that the essential change in the concentration of the inorganic constituents is in the calcium and that this change is constant. The sodium is normal in amount. There is frequently a slight increase in the potassium, but this is not regular. The concentration of magnesium is essentially unaltered.

Biedermann,[9] in 1881, observed the rhythmical contraction of striated muscle produced by chemical stimulation (curarized sartarius muscle of frog at 10 C.) in a solution which contained: NaCl, 5.0; Na_2HPO_4, 2.0; Na_2Co_3, 0.4-0.5 gm. per liter. After a shorter or longer period of rest he observed contractions which varied in intensity. Loeb [10] studied the effect of many salts on the sartorius muscle of the frog. The salts included sodium chlorid, sodium bromid, sodium iodid, sodium acetate, fluorid, formate, succinate, sulphate, sodium bicarbonate, sodium oxalate, sodium phosphate and sodium citrate. The minimal stimulating concentration of sodium chlorid is M/16.

TABLE 2.—Concentration of Sodium, Potassium and Calcium in the Serum of Infants with Active Tetany—Expressed as mgm. per 100 c.c.

	Age	Na	K	Ca
G. C.	7 months	330	29	5.7
W. B.	6 months	337	27	7.2
M. J.	3 years	322	19	4.6
A. H.	5 months	320	23.7	5.1
O. G.	7 months	324	23.1	6.0

The concentration of sodium in serum is N/7. The concentration of chlorin in serum is also N/7 and that of [HCO_3] is 0.032 or about N/30. The effect of the salts is due not only to the cation sodium but also to the anion. For instance, sodium phosphate M/128 is as effective as sodium chlorid M/16, and sodium bicarbonate M/16-M/32 is as effective as sodium chlorid M/16. In isoosmotic solutions potassium does not have the same effect as sodium. Mines [12] has shown that when the concentration of potassium is approximately that of the serum it reinforces the effect of the sodium.

Loeb [10] has further shown that when to a solution of sodium bromid (isoosmotic with sodium chlorid 0.7 per cent.) a quantity of calcium chlorid is added making the total calcium concentration 10 mg. per hundred c.c. of solution, weak contractions appeared for only thirty minutes after which time the muscle was absolutely quiet. This has been confirmed by others. This is, therefore, the minimum concentration of calcium for protection against the stimulating effect of sodium. So that Loeb [14] states, "We are, therefore, indebted to the calcium concentration of our blood that our muscles do not constantly twitch."

14. Loeb, J.: Handbuch der Biochemie des Menschen und der Tiere, C. Oppenheimer, **2**: Pt. 1, 124. Gustav Fischer, Jena, 1910.

Loeb [15] assumed that sodium ions penetrate the muscle cell and replace the calcium, bringing about a disturbance of the equilibrium between sodium, potassium and calcium, but he did not explain the mechanism of the penetration. Later Loeb [16] has shown that univalent cations can penetrate the cell membrane, and enter the cell only when conditions are such as to favor the formation of protein-cation compounds with the protein of the cell membrane. The most important of these conditions is that the p_H of the solution should be above the isoelectric point of the protein. In the presence of divalent cations these compete with the univalent cations for the protein and a much weaker concentration of divalent cations will protect against the effect of monovalent cations. Thus a concentration of calcium chlorid above M/512 will prevent the formation of sodium gelatinate in a sodium chlorid solution of a concentration of M/8 or M/4, the concentration of sodium chlorid in normal serum being M/7. These facts have been used by Loeb to explain the phenomena of antagonistic salt action between salts with monovalent and divalent cations on the irritability of muscles and nerves. Attention should be called to the fact that a concentration of calcium chlorid M/512 corresponds to about 7.8 mg. calcium per hundred c.c. of solution—considerably lower than that found in normal serum and only a little above the concentration of calcium which may be found with tetany.

Sabbatani [17] showed that the direct application to the surface of the brain of salts whose anions precipitate calcium causes an increase in the irritability of the cortex. MacCallum, Lambert and Vogel [18] have shown that when the extremity of a dog is perfused with defibrinated blood, part of the calcium of which has been removed by dialysis, the excitability of the nerves to the galvanic current is greatly increased. Keith-Lucas [19] has shown from certain theoretical considerations based on his own work and that of Nernst,[20] Hill [21] and Mines [12] that the minimal stimulus required to produce excitation of the nerve increases as the amount of calcium in the solution bathing the nerve is increased. Matthews [11] and Loeb [15] showed that when the nerve of a nerve-muscle preparation is immersed in a solution which precipitates calcium, the muscle twitches. When calcium is added to the solution the twitching is completely inhibited if the calcium reaches a concentration of 10 mg.

15. Loeb, J., and Ewald, W. F.: J. Biol. Chem. **25**:377, 1916.
16. Loeb, J.: J. Biol. Chem. **34**:77, 1918.
17. Sabbatani: Funzione biologica del Calcio, Accad. Reale dille Scienze di Torino, 1904.
18. MacCallum, W. G., Lambert, R. A., and Vogel, K. M.: J. Exper. M. **20**:149, 1914.
19. Keith-Lucas: J. Physiol. **40**:225, 1910.
20. Nernst, W.: Arch. f. d. ges. Physiol. **122**:275, 1908.
21. Hill, A. V. J.: Physiol. **40**:190, 1910.

per hundred c.c. of solution, while there is no inhibition or only incomplete inhibition if the concentration of calcium is 5 mg.

The experiments of Loeb, Mines, Matthews and others were performed on nerves and muscles of cold blooded animals. It is, however, to be emphasized that the concentrations of sodium, potassium, calcium and magnesium which produce normal conditions in these structures are essentially the same as the concentrations of these elements in the blood of normal infants. When the concentration of calcium is reduced to the level which is found in infantile tetany, that of the other elements remaining unchanged, a great increase in the irritability of the neuromuscular mechanism results.

We have found the concentration of the sodium, potassium and magnesium in the serum of patients with tetany essentially normal. On the other hand, the concentration of the calcium is regularly lowered. Obviously, the important factor in increasing the irritability of the neuromuscular mechanism in infantile tetany is the decrease in the calcium concentration. The stimulating effect of the sodium and potassium salts is unopposed by the inhibitory effect of calcium.

CONCLUSIONS

In infantile tetany the inorganic phosphorus of the serum shows a marked variation. In about half the cases the concentration is normal or slightly above normal. An increase in the inorganic phosphorus of the serum does not seem to be responsible for infantile tetany. The ratio $\frac{\text{Na and K}}{\text{Ca and Mg}}$ is increased. This is almost wholly due to a decrease in the concentration of calcium. The concentration of sodium and magnesium is essentially normal; that of potassium is slightly increased.

The increased irritability of the neuromuscular mechanism, which is the essential phenomenon in infantile tetany, is due to the diminution of the concentration of calcium in the serum.

EXPERIMENTAL ALBUMINURIA IN THE RABBIT*

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It is a well recognized fact that the excretion of albumin in the urine occurs in circulatory disturbances of the kidneys. As the kidney is very sensitive to circulatory disorders, albuminuria may occur (except in nephritis) either because of local congestion of the veins and capillaries, or because of anemic infarct of the kidney. It may also occur in the course of general anasarca due to obstruction.

As stated by Jehle,[1] lordosis is the chief cause of orthostatic albuminuria. Venous hyperemia of the kidney is brought on by faulty position of the lumbar spine. This observation was confirmed by animal experiments, which have since been repeated by many investigators.

Menge [2] employed massage of the kidney in twenty-one instances; in fifteen the presence of albuminuria was confirmed. Zebrowski and Glewitsch [3] attempted to electrify the kidney with the faradic current in thirty-three cases. They found albuminuria in only one case. Gomolitsky,[4] in the case of thirty-five patients suffering from a floating kidney, tried to stimulate the kidney by various measures, such as pressure, massage and the faradic current. He found albuminuria in eight cases.

Cohn [5] experimented on the rabbit. He found that a trace of albumin appeared in the urine after four hours by massaging the kidney for one minute. A small amount of red blood corpuscles, and a slight quantity of albumin, were found after two minutes massage. An abundance of albumin (0,25 o/oo) appeared after three minutes massage; and albumin, (0,5 o/oo) red blood cells, leukocytes, epithelial cells, hyalin and granular casts appeared after five minutes massage. After ten minutes massage, the albumin in the urine increased (1,0 o/oo); many casts and cylinders appeared and were present for several days. Fischl [6] confirmed the importance of lordosis

* Received for publication, May 26, 1921.

1. Jehle, L.: Die lordotische Albuminurie, Leipzig and Wien., 1909; Die Albuminurie, Ergebnisse d. Inn. Med. u. Kinderh. **12:** 1913.

2. Menge: Ueber Urinbefund nach Nierenpalpation, Münch. med. Wchnschr. 1900.

3. Zebrowski u. Glewitsch: Ueber faradische Albuminurie, Russki Vratsch, No. 22, 1907; Ref. Ztschr. f. Urol., 1908.

4. Gomolitsky: Beiträge zur Lehre von der orthostatischen Albuminurie, Ztschr. f. klin. Med. **77:** 1913.

5. Cohn: Zur renalpalpatorischen Albuminurie, Ztschr. f. Urol. **6:** 1912.

6. Fischl: Weitere Mitteilungen über mechanische Erzeugung von Albuminurie u. Nephritis bei Tieren, Monatschr. f. Kinderh. **9:** 1911; Ztschr. f. Exper. Path., 1912.

as a cause of albuminuria by experiments on animals. When rabbits and dogs were kept in exaggerated lordosis, albumin, casts and red blood corpuscles appeared in the urine. The kidney in such cases, examined pathologically, resembled the kidney of paedonephritis.

Summarizing all the reports by many investigators (Schreiber,[7] Seelig,[8] and others) it seems that the appearance of the so-called "renalpalpatoric or abdominalpalpatoric" and "lorditic albuminuria" is variable in human beings as well as in animals.

TABLE 1.—The Left Kidney Was Manipulated Through the Abdominal Wall So as to Interrupt the Blood Circulation. The Results Made Apparent in the Urine Are Shown

Time Pressed	Rabbit Number	Urine				
		Acetic Acid Body	Albumin	Blood-cells	Cylinder	Sugar
1 Minute	1	(—)	(—)	(—)	(—)	(—)
1 Minute	2	(—)	Trace	(—)	(—)	(—)
1 Minute	3	(—)	(—)	(—)	(—)	(—)
1 Minute	4	(—)	Trace	(—)	(—)	(—)
2 Minutes	5	(—)	(—)	(—)	(—)	(—)
2 Minutes	6	(+)	Trace	(—)	(—)	(—)
3 Minutes	1	(—)	0 2 o/oo	(—)	cylindloid	(—)
3 Minutes	2	(—)	0 066 o/oo	(—)	cylindloid	(—)
3 Minutes	3	(—)	0 066 o/oo	(—)	(—)	(—)
3 Minutes	4	(+)	Trace	(—)	(—)	(—)
3 Minutes	5	(+)	0.066 o/oo	(—)	(—)	(—)
5 Minutes	1	(+)	Trace	(—)	hyalin cyl'nders	(—)
5 Minutes	2	(—)	0.1 o/oo	(+)	(—)	(—)
5 Minutes	3	(+)	0 033 o/oo	(—)	(—)	(—)
5 Minutes	4	(+)	0 1 o/oo	(—)	(—)	(—)
5 Minutes	5	(+)	0 066 o/oo	(—)	(—)	(—)
10 Minutes	6	(+)	1,5 o/oo	(—)	granular cylinders	(—)
15 Minutes	1	(+)	0,5 o/oo	(+)	(—)	(—)
15 Minutes	2	(+)	2.0 o/oo	(+)	granular cyl'nders	(—)
15 Minutes	3	(—)	0,033 o/oo	(—)	(+)	(—)
15 Minutes	4	(+)	0,033 o/oo	(+)	(—)	(—)
15 Minutes	5	(+)	3 0 o/oo	(—)	(+)	(—)
15 Minutes	6	(+)	2,0 o/oo	(—)	(—)	(—)
15 Minutes	7	(+)	1,5 o/oo			
15 Minutes	8	(+)	0,66 o/oo	....	(+)	(—)
15 Minutes	9	(+)	0,33 o/oo	(+)	(+)	(—)
20 Minutes	10	(+)	0,50 o/oo	(—)	(+)	(—)
20 Minutes	11	(—)	2,0 o/oo	(—)	(+)	(—)

In our experiments, we applied mechanical, thermal and electrical irritations to left kidney of the rabbit. We then exercised pressure on the kidney with four fingers within the abdominal wall for different periods of time so as to produce some obstruction or hyperemia of the kidney. Furthermore, we exposed the left kidney, and ligated the renal artery and vein separately, for different times. The animal was catheterized after thirty or sixty minutes, and the urine was examined chemically and microscopically. Before each experiment the catheterized urine was normal.

7. Schreiber: Ueber flüchtige Albuminurie, Med. Klin., No. 14, 1909; Ueber renalpalpatorische Albuminurie, Ztschr. f. klin. Med. **55**:1911.

8. Seelig: Ueber renalpalpatorische Albuminurie, Ztschr. f. Urol. **3**: 1909.

The chief object of the experiment was to ascertain whether albumin will come from intact kidney. On account of the small size of the ureter of the rabbit our object could not be attained. Both kidneys were removed soon after manipulation and examined pathologically.

PROTOCOLS OF EXPERIMENTS

1. *Experiment on the Relationship Between the Appearance of Albuminuria and the Circulatory Interruption and Also the Irritation of the Kidney of One Side.*—As shown in Table 1, a trace of albumin

TABLE 2.—RESULTS OF MASSAGE OF THE LEFT KIDNEY

Rabbit No.	Duration of Massage	Urine				
		Acetic Acid Body	Albumin	Blood-cells	Cylinder	Sugar
1	2 Minutes	(—)	(—)	(—)	(—)	(—)
2	5 Minutes	(—)	(—)	(—)	(—)	(—)
3	5 Minutes	(—)	(—)	(—)	(—)	(—)
4	10 Minutes	(+)	0,1 o/oo	Scanty	Granular cylinder scarcely	(—)
5	10 Minutes	(—)	(—)	(—)	(—)	(—)
6	10 Minutes	(—)	0,033 o/oo	(—)	(—)	(—)
7	10 Minutes	(—)	(—)	(—)	(—)	(—)
8	10 Minutes	(—)	(—)	(—)	(—)	(—)

TABLE 3.—RESULTS OF EXAMINATION OF URINE IN LORDOSIS

Rabbit No.	Duration	Urine				
		Acetic Acid Body	Albumin	Blood-cells	Cylinder	Sugar
1	10 Minutes	(—)	Trace	(—)	(—)	(—)
2	10 Minutes	(—)	(—)	(—)	(—)	(—)
3	15 Minutes	(—)	(—)	(—)	(—)	(—)
4	18 Minutes	(—)	(—)	(—)	(—)	(—)

TABLE 4.—RESULTS OF COOLING THE LEFT KIDNEY THROUGH THE ABDOMINAL WALL

Rabbit No.	Duration of Cooling	Urine				
		Acetic Acid Body	Albumin	Blood-cells	Cylinder	Sugar
1	10 Minutes	(+)	(—)	(—)	(—)	(—)
2	20 Minutes	(+)	Trace	(—)	(—)	(—)
3	20 Minutes	(+)	0,033 o/oo	(—)	(—)	(—)

sometimes appears in the urine after the application of pressure on the inside of the left kidney for one or two minutes, but no blood cells and cylinders.

Albumin is found in all cases after applying pressure for more than three minutes. Casts, blood cells and cylinders appear in a large majority of cases after exercising pressure for more than ten minutes.

If the kidney is massaged for less than five minutes no albumin appears. It may appear sometimes after massaging the kidney for more than ten minutes. Cooling the kidney for twenty minutes with an ice bottle through the abdominal wall seldom causes a slight albuminuria. Lordosis of the lumbar spine as well as irritation of the kidney with the faradic current provoke no changes in the urine (Tables 2, 3, 4 and 5).

2. Pathological Changes of Both Kidneys When the Stimulus is Given Directly on One Side.—The left kidney was exposed through a laparotomy, the blood vessels were ligated for varying periods and

TABLE 5.—RESULTS OF FARADIZATION OF THE LEFT KIDNEY THROUGH THE ABDOMINAL WALL (ROLL-DISTANCE, 6 CM.)

Rabbit No.	Duration	Urine				
		Acetic Acid Body	Albumin	Blood-cells	Cylinder	Sugar
1	10 Minutes	(—)	(—)	(—)	(—)	(—)
2	20 Minutes	(—)	(—)	(—)	(—)	(—)

TABLE 6.—POSTMORTEM COMPARISON OF BOTH KIDNEYS

Rabbit No.	Management	Left Kidney		Right Kidney	
		Weight, Gm.	Congestion (Macroscopically)	Weight, Gm.	Congestion (Macroscopically)
	Ligature of left vena renalis				
1	10 minutes	9.3	+++	6.5	+
2	20 minutes	8.5	++	5.5	+
3	20 minutes	14.9	+++	6.3	+
4	30 minutes	10.5	+++	5.2	+
	Ligature of left artery				
5	10 minutes	5.8	+++	5.0	+++
6	20 minutes	6.5	+++	5.3	++
	Ligature of both artery and vein				
7	20 minutes	7.8	+++	5.9	—
	Cooling of left kidney				
8	20 minutes	7.0	—	6.3	—
	Massage of left kidney				
9	20 minutes	7.5	+	7.0	—
10	20 minutes	5.5	++	5.0	—
	Faradization of left kidney				
11	30 minutes	5.3	—	5.2	—
12	30 minutes	5.2	—	5.4	—

massage, pressure and electrical irritation were directly applied to the kidney. After thirty minutes both kidneys were removed, weighed and examined macroscopically as well as microscopically. The findings are summarized in Table 6.

It has been demonstrated that, when congestion takes place macroscopically in one side, the same products are found more or less in the other untouched kidney. The characteristic change in the kidney that shows congestion is a notable swelling, with rubbery hardness. The whole organ is of a deep purplish color. Microscopically, all the capillaries, especially of the glomeruli, are filled with blood cells. Distension, epithelial desquamation and destruction in Bowman's capsules

or in the tubules are scarcely seen. The picture in short, is that of an acute congestion. The untouched right kidney shows the same changes, when the other kidney is in a state of congestion. No fat infiltration was noticed.

CONCLUSIONS

1. A trace of albumin sometimes appears in the urine when the kidney is massaged through the abdominal wall for one or two minutes; it occurs always after applying pressure for more than three minutes. Besides, albumin, casts, blood cells and cylinders appear in the urine in a majority of cases when the pressure is applied for more than ten minutes.

2. No constant relationship exists between the appearance of albuminuria and massage, cooling, lordosis or faradic irritation of the kidney.

3. When congestion is provoked in a kidney mechanically, it occurs also in the other kidney to a certain degree. Whether this is a reflex phenomenon, or whether it is permanent, remains to be investigated.

THE VITAL CAPACITY OF THE LUNGS AND ITS RELATION TO EXERCISE TOLERANCE IN CHILDREN WITH HEART DISEASE

STANDARDS FOR NORMAL VITAL CAPACITY FOR CHILDREN. THE LUNG CAPACITY IN CERTAIN INTRATHORACIC CONDITIONS *

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In children with heart disease a knowledge of the capacity for physical activity is an essential part of the final diagnosis. There are numerous factors involved in the circulatory dynamics, however, which make an estimate of the functional capacity difficult; for this reason it has seemed desirable to make measurements of other functional processes.

The close interrelationship of the circulatory and respiratory functions in man is well shown by the marked disturbances in breathing exhibited by patients with failing cardiodynamics. Most of the studies on vital capacity are based on this fundamental relationship of function, and the attempt is made to give expression in a quantitative way of the degree of circulatory involvement by noting the altered ability on the part of the subject to take a deep breath and then to expel it completely. A number of studies [1] have been made using the vital capacity as a criterion of the functioning of the circulatory mechanism, and all have indicated a close relation between the clinical picture and the degree of reduction in the vital capacity.

Considerable attention of late has been given to the matter of cardiac functional efficiency, and in the tests of Stone,[2] Barach,[3] Barringer,[4] Schneider,[5] Wilson [6] and others we have attempts to give in different ways an objective expression of the heart's functional capacity. It is not our purpose to discuss here the relative merits of the different

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1. McClure and Peabody: J. A. M. A. **69**:1954 (Dec. 8) 1917; Peabody and Wentworth: Arch. Int. Med. **20**:443 (Sept.) 1917; Levine and Wilson: Heart, **7**:53, 1919.
2. Stone: J. A. M. A. **71**:1256 (Oct. 4) 1913.
3. Barach: J. A. M. A. **72**:525 (Feb. 14) 1914.
4. Barringer: Arch Int. Med. **20**:829 (Dec.) 1917.
5. Schneider: J. A. M. A. **74**:1507 (May 29) 1920.
6. Wilson: Am. J. Dis. Child. **20**:188 (Aug.) 1920.

tests; we simply wish to indicate that the determinations of the exercise tolerance, as previously reported,[7] has seemed to afford the best measure of the cardiac factor in the evaluation of the physical fitness of the subjects studied in this research. The aim of the observations here reported was to determine to what extent measurements of the vital capacity, as an expression of one aspect of the respiratory function, can be correlated with the exercise tolerance test as a form of measurement of cardiac functional capacity.

METHOD

The vital capacity measurements were all made with a bellows type spirometer similar in principle to that described by Krogh.[8] The instrument was equipped with a double counter-weighting system which rendered it equally sensitive for the entire range of the measurements taken. The connection to the patient was made by means of a five-eighth inch rubber tube with fiber mouth pieces of the same diameter. The total capacity of the spirometer was about 9½ liters.

All observations were made on the subjects in the sitting posture, and particular attention was given to the matter of having a free and comfortable attitude at the time the readings were made. It was the practice to take five observations at a sitting, but often as many as ten observations were taken before a degree of constancy could be obtained which satisfied the requirement of the method. Moreover, in many cases, our observations have been checked by having the patient return for another test at a later date, and as many as eight of these repeated tests have been made on some of the subjects. Special precautions need to be taken in young subjects, such as used in this study, to see that normal breathing is maintained previous to the test of vital capacity. We have observed in many children a tendency to hold the breath while the observations were being made. This appears to have been due mainly to a mental state elicited by our instructions to the subject to make the greatest effort possible to fill the lungs completely before blowing into the spirometer.

The readings on the scale of the instrument were taken usually to the nearest 50 c.c., and the highest figure attained out of the five or more observations made at a sitting was taken for the computation of values.

The exercise tolerance tests used were those of the table of standardized test exercises previously reported.[7] The degree of distress and type of change in the systolic blood pressure following these test exercises were taken as a gauge in estimating the tolerance which was reported under one of three headings—normal, diminished, or poor.

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7. Wilson: J. A. M. A. **76**:1629 (June 11) 1921.
8. Krogh: Skand. Arch. f. Physiol. **27**:100, 1912.

Standards for Normal Vital Capacity.—Our standard for normal vital capacity was obtained from a study of eighty-five subjects; forty-four boys and forty-one girls. The age range of these subjects was from 6 to 16 years; they were in apparent good health and were regularly attending public school. In selecting the subjects for this group special care was taken to rule out all cases giving clinical or ausculatory signs of heart or lung disease, as well as those whose mental status rendered them unfit to perform the test satisfactorily. Moreover, exercise tolerance tests were made on a large number of the cases to assist in deciding the physical fitness of the subjects. On the other hand, an effort has been made to have this group a representative one in the sense that it fairly embodies a cross section of the age, general health, and home environment of the children of the locality in which these studies were made.

Very few observations have been recorded concerning the vital capacity of children. Stiles and Graves [9] report a study on a large number of children between the ages of 6 and 17, but their figures are related entirely to age which renders them of little use as standards of measurements. At the outset, therefore, it was necessary to establish, first, accurate standards for relating the vital capacity measurements; and second, measurements of normal children to determine the average normal range of variation.

Dreyer [10] has concluded from his studies on physical relationship that there is no correlation between age, weight, and height. On the other hand, he [11] has shown that a definite relationship exists between certain body measurements and the vital capacity. In adults the matter of standards for normal vital capacity has been studied by West,[12] and he concludes from an extensive comparison of the different methods in use to express this measurement in a comparative way, that the one based on vital capacity per square unit body surface fulfills the requirements in a satisfactory manner.

We have adopted in this study the form of expressing the vital capacity on the basis of a square meter body surface, the latter being determined from the height-weight chart of Dubois and Dubois.[13] Before accepting this, however, as our standard form of expression, we made chest circumference and stem length measurements on a group of 32 children, according to the methods used by Dreyer.[10] The vital capacity was then calculated from these measurements, using the Dreyer tables for this purpose.

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9. Stiles and Graves: U. S. Public Health Reports, Reprint 306, 1915.
10. Dreyer: The Assessment of Physical Fitness, Cassill & Co., London, 1920.
11. Dreyer: Lancet **2**:227 (Aug. 9) 1919.
12. West: Arch. Int. Med. **25**:306 (March) 1920.
13. Dubois, D. and E. F.: Arch Int. Med. **15**:868 (June) 1915.

In Table 1 are shown the results so arranged as to indicate in a comparative way three different modes of expressing the vital capacity values as based on certain body measurements.

The values shown in this table were derived in the following manner. In the first column the figures represent the percentage difference between the vital capacity actually observed and that calculated from Dreyer's tables. A calculated vital capacity means the average of the values obtained from Dreyer's tables for the observed chest circumference and stem length. This calculated value was then taken as the standard of normal for a particular set of bodily measurements, and

TABLE 1.—A Comparison of Different Methods of Expressing Vital Capacity as Related to Body Measurements

Subject	Age	Weight, Kg.	Height, Cm.	I Chest Circumference and Stem Length	II Body Weight	III Surface Area, Per Cent. of Average Normal
a 1A N	11	31	132	+29	+17	126
a 2B I	11	34	145	+ 9	+11	94
a 3B I	11	39	144	−12	− 4	102
a 4C I	..	36	131	−23	−22	77
a 5C I	9	26	128	0	+ 4	96
a 6C I	12	39	158	+ 3	+ 1	90
a 7C I	10	27	127	−16	− 6	89
a 8C I	6	20	117	−30	−29	70
a 9D I	10	41	152	−14	−12	88
a10D I	12	42	152	+ 8	+ 9	98
a11D I	15	48	158	−31	+ 1	93
a12F I	13	33	146	− 1	+ 8	100
a13G I	11	27	136	+ 1	+ 8	97
a14H I	..	20	119	−17	−11	79
a15K N	..	31	143	−17	−12	88
a16K I	12	42	145	+ 1	+ 3	110
a17M I	..	21	122	−10	− 5	84
a18M I	9	27	136	−13	−17	75
a19M I	14	42	143	−17	− 9	99
a20M I	16	55	171	+17	+19	122
a21M I	10	21	127	−13	− 8	81
a22O I	9	33	136	+ 5	− 3	105
a23P N	9	23	116	− 6	− 6	100
a24P I	..	26	145	−26	− 1	83
a25P I	12	55	156	−20	−22	85
a26R I	10	20	125	−27	−27	63
a27S I	..	31	140	− 6	−12	92
a28S I	..	38	165	−14	+ 5	90
a29T I	15	57	164	−15	−16	82
a30V N	..	32	138	+12	+10	110
a31W I	9	28	131	−12	− 8	96
a32W I	..	30	137	−13	−75	78

the vital capacity observed is here expressed as a percentage deviation from the calculated. In the second column the figures represent the percentage difference between the observed vital capacity and that given in Dreyer's tables for the body weight observed. Both these forms of expression follow in all essentials the method described by Dreyer. The figures in the third column are based on a surface area relation. It represents the percentage change from a value which we have established in this study as the average normal vital capacity per square meter body surface.

A comparison of the values given under these three modes of expressing the results reveals a close agreement between them. With few exceptions the differences are in the same direction and show a proportionality within the limits of error of the methods employed. We have, therefore, adopted the surface area mode of expressing the results since it gave values in general comparable to the other methods, and possesses the additional advantage of utilizing measurements which are susceptible, we believe, of greater accuracy when made on children.

The result of the observations shown in Table 2 is that the average vital capacity for boys is 1,902 c.c. for each square meter of body surface, and 1,837 c.c. for girls for the same unit surface area. When the average is taken for the boys and girls together, the value 1,870 c.c. per square meter body surface is obtained, and applying this to the entire group, it is evident that 67 per cent. of the subjects come within a plus or minus 10 per cent. deviation. The lowest individual reading observed was 1.41, and the highest 2.50 L. per unit surface. These wide limits of variation are due, we believe, in part, to the large experimental error in taking such measurements on children, and, in part, to other factors, such as differences in physical vigor and certain intrathoracic conditions not revealed by physical examination. The latter factor will be considered in some detail in another part of this paper.

It is of interest in passing to note that the same vital capacity measurement when related to the body weight alone, as shown in the last column of Table 2, exhibits a slightly less constancy (65 as against 67 per cent.) then when related to a unit surface area. This difference, however, cannot be considered significant in view of the relatively great variation which measurements of this sort contain.

An attempt was made to arrange the vital capacity data into certain groups with respect to body height; the first group to contain all subjects under 4 feet 3 inches; the second group, subjects 4 feet 3 inches to 4 feet 7 inches; the third group, subjects 4 feet 7 inches to 5 feet; and the fourth group all subjects over 5 feet. The great degree of variability exhibited by the figures obtained made it evident that such a method possessed no practical value.

We have also observed a few young subjects of from 5 to 8 years and of small stature measuring 0.85 sq. m. or less. In these we have obtained a consistently low vital capacity. The figures for the five cases we have observations on range from 18 to 30 per cent. below the average. It has not been possible for us to determine whether this difference is in fact a constitutional one, or is simply an error in the surface area method when applied to so small subjects. The fact that we have others just as young, but of larger stature, giving a normal value favors the interpretation that it is not a matter of age difference.

TABLE 2.—VITAL CAPACITY OF NORMALS

Case No.	Age	Weight, Kg.	Height, Cm.	Liters per Sq. M. Surface		Vital Capacity, C.c.	Liters per Kg. Body Weight	Percentage Difference Between Observed and Calculated	
				Boys	Girls			Boys	Girls
1 A	7	27	131	1.97	....	1,975	0.71	+45	
2 A	11	31	132	2.34	....	2,500	0.81	+17	
3 A	10	30	141	....	1.86	2.050	0.68	....	+13
4 B	10	31	136	....	1.83	2,000	0.64	....	+ 7
5 B	9	24	128	2.02	....	1,900	0.78	+22	
6 B	8	32	132	2.18	....	2,350	0.71	+22	
7 B	8	25	125	1.60	....	1,500	0.59	—18	
8 B	12	34	123	....	1.87	2,300	0.66	....	+14
9 B	6	23	129	1.77	....	1,650	0.70	— 6	
10 C	11	33	117	....	1.96	2,300	0.68	....	+17
11 E	13	45	160	....	1.83	2,625	0.58	....	+ 8
12 E	10	29	135	2.28	....	2,400	0.81	+17	
13 E	10	30	128	....	1.75	1,800	0.58	....	— 1
14 G	10	39	142	1.78	....	2,200	0.56	—12	
15 G	15	50	158	....	1.62	2,575	0.51	....	— 2
16 G	7	19	111	....	1.87	1,400	0.52	....	—10
17 G	7	24	122	1.76	....	1,600	0.64	— 6	
18 G	10	33	140	....	1.93	2,200	0.66	....	—13
19 G	8	24	127	1.95	....	1,800	0.73		
20 H	10	35	140	2.18	....	2,600	0.74	—28	
21 H	7	21	126	1.62	....	1,425	0.67	—18	
22 H	6	26	125	1.90	....	1,800	0.69	— 4	
23 H	11	36	148	....	1.68	2,100	0.59	....	+ 2
24 H	10	29	137	2.00	....	2,100	0.72	+ 4	
25 H	10	35	141	....	2.02	2,400	0.68	....	+19
26 I	9	37	137	1.58	....	1,600	0.50	—32	
27 K	14	45	152	....	1.81	2,250	0.56	....	+ 5
28 K	12	32	142	....	1.82	2,000	0 67	....	+15
29 K	11	31	143	1.68	....	1,900	0.60	—12	
30 L	12	39	132	1.81	....	2,350	0.59	— 7	
31 L	8	29	129	1.69	....	1,725	0.59	—14	
32 L	8	25	122	1.75	....	1,625	0.63	—12	
33 L	11	31	137	....	1.88	2,025	0.66		
34 L	10	35	167	1.55	....	2,025	0.68	—12	
35 M	9	31	132	....	1.59	1,700	0.53	....	— 9
36 M	12	40	140	1.41	....	1,800	0.44	—19	
37 M	13	48	152	....	1.97	2,800	0.58	....	+10
38 M	7	28	128	....	1.70	1,700	0.60	....	+ 5
39 B	11	38	142	....	1.89	2,300	0.60	....	+ 7
40 M	10	36	141	....	1.83	2,200	0.59	....	+ 5
41 M	7	38	134	2.02	....	2,400	0.63	— 2	
42 M	13	34	149	2.50	....	2,900	0.87	+27	
43 M	9	28	134	....	1.94	2,000	0.70	....	+15
44 M	7	24	118	1.82	....	1,600	0.66	— 9	
45 M	12	28	125	....	1.73	1,700	0.60		
46 M	10	28	122	2.09	....	2,025	0.72	+ 2	
47 M	11	36	165	1.87	....	2,350	0.74	+14	
48 M	9	27	132	....	1.97	1,975	0.69	....	+19
49 M	10	34	133	....	2.14	2,400	0.69	....	+19
50 O	14	54	165	....	1.88	3,000	0.55	....	+12
51 O	10	29	135	1.86	....	1,975	0.66	— 4	
52 P	8	22	116	1.90	....	1,600	0.70	— 6	
53 P	15	58	161	....	1.61	2,600	0.64	....	+ 6
54 O	13	29	137	....	1 76	1,900	0.50	....	— 7
55 P	11	45	142	....	1.73	2,300	0.50	....	— 7
56 R	9	27	134	1.62	....	1,625	0.59	—16	
57 R	11	31	139	....	1.45	1,600	0.51	....	—14
58 R	9	21	119	1.93	....	1,600	0.74	— 2	
59 R	15	38	138	2.20	....	2,650	0.68	+ 9	
60 S	11	35	140	....	1.61	1,900	0.53	....	— 7
61 S	10	28	128	....	1.87	2,000	0.69	....	+14
62 S	9	27	128	2.12	....	2.050	0.74	+ 6	
63 S	12	34	147	....	2.00	2,400	0.69	....	+20
64 S	11	24	131	1.95	....	1,875	0.77	+ 5	
65 S	12	33	135	2.00	....	2,200	0.74	— 1	
66 S	8	23	124	....	1.56	1,400	0.60	....	— 7
67 S	12	36	147	....	2.10	2,375	0.71	....	+25
68 T	9	36	147	1.95	....	2,400	0.65		
69 B	10	32	138	2.16	....	2,400	0.74	+10	
70 W	12	36	146	....	1.98	2,400	0.65	....	+15
71 Z	10	35	145	....	1.77	2,125	0.60	....	+ 5
72 G	9	24	90	....	2.32	1,533	0.69	....	— 8
73 L	12	37	145	....	1.68	2,094	0.55	....	+ 2
74 D	13	41	152	....	1.74	2,255	0.56	....	+ 2
75 L	13	42	150	....	1.59	2,294	0.50	....	— 8
76 C	10	26	130	1.94	....	1,868	0.73	+ 2	
77 M	14	46	150	....	2.01	2,450	0.57	....	+ 6
78 S	9	28	127	2.40	....	1,970	0.86	+22	
79 D	13	29	151	1.74	....	2,021	0.69	— 1	
80 T	10	37	142	1.83	....	2,408	0.60	— 9	
81 D	9	29	130	1.86	....	2,021	0.66	— 6	
82 L	7	20	120	1.61	....	1.547	0.68	—13	
83 D	6	20	93	1.94	....	1,547	0.65	—16	
84 S	13	30	140	....	2.17	2,071	0.74	....	+15
85 M	7	18	115	1.67	....	1,436	0.73	— 9	
Average.	.....	.....	.....	1.90	1.84	.....	0.64		

The Group with Heart Disease.—One hundred and sixty-six patients with heart disease, sixty-three boys and 103 girls, were selected for this study, so as to include all manifestations of organic heart disease; congenital and acquired as well as a potential group. The subjects with organic heart disease have been divided into three main classes on the basis of exercise tolerance, as determined by the reaction to the standardized test exercise. The relation of the determination of vital capacity to the exercise tolerance will be considered respectively for each class.

In Class 1 there are included eighty-eight children with organic heart disease having a normal exercise tolerance; that is, they are able to tolerate an average or a severe standardized test exercise.[7] These children attended school, enjoyed and tolerated free play and were quite normal in their general activity. Seventy-three of these subjects had mitral lesions; two with combined mitral and aortic, and thirteen with congenital cardiac malformation. The general development and nutrition of this group compared favorably with the average normal subjects.

The vital capacity observations for this series shows an average value for the thirty boys of 1,910 c.c., and for the fifty-eight girls of 1,789 c. c. per sq. m. surface area. The combined average is 1,830 c. c., a figure which is only about 2 per cent. below the average obtained for the normal group. The lowest observation was 1,300 c. ., and the highest 2,380 c. c., values which show a degree of variation quite similar to that exhibited in our normal group of subjects. It is of interest also to observe that the vital capacity measurements of this group corroborates the classification which is based upon excerise tolerance.

In Class 2 are included a total of thirty-eight children with organic heart disease. All of these subjects were shown to have a diminished exercise tolerance; that is, they were only able to tolerate a moderate standardized test exercise. This group, while ambulatory, represents two degrees of diminished tolerance. The clinic group of twenty children included subjects convalescent from cardiac failure, as well as those who had been unduly restricted and had been in bed for prolonged periods. The second or hospital group of eighteen children were more especially of the latter type, since they came directly from the hospital wards.

The data on the vital capacity we have arranged, therefore, in two parts. In the first part are the observations on sixteen girls and four boys, subjects taken from the same locality as our normal and Class 1 cases, and showing a combined average vital capacity for the boys and girls of 1,405 c. c. per sq. m. surface area. In the second part of this series are the observations on fifteen boys and three girls who were at

the time patients in the Mineola Home for Cardiac Children. This series of boys and girls gave a combined average vital capacity of 1,368 c. c. per sq. m. surface. There is shown in the final average figures for these two series a significantly lower value for the Mineola group. Another feature in this comparison not to be lost sight of is the fact that the hospital series of cases were all selected and were without exception the worst of their class.

It is evident, therefore, that the two series considered under this class are not strictly comparable; one part embodies essentially representative subjects, the other part a selected lot of subjects from the lower range of the class. But it is significant to note that both parts give average values much below that obtained for the normal group, and that the two series considered together show an average vital capacity of 26 per cent. below the average normal.

Repeated determinations of the vital capacity on ten of the subjects of this class taken over a period of one to six months have shown that clinical improvement and greater tolerance is accompanied by an increase in the vital capacity measurement.

In Class 3, we have made observations on only five subjects. These were all bed cases with cardiac failure and were unsuitable, therefore, to give an exercise tolerance test.

The vital capacity determinations had to be taken with the greatest care as the effort required provoked coughing attacks which interfered with the satisfactory performance of the test. It cannot be claimed that the readings fairly represent the lung capacity because of this inability to properly fill or empty the lungs. But the chief interest in these results lies not so much in the absolute degree of reduction exhibited by this class as a whole, as in the striking relation shown between the clinical picture and the reduced vital capacity findings. Four of these cases showed a vital capacity less than 50 per cent. of the average normal, and all were marked cases of cardiac failure. The fifth case showed about 30 per cent. reduction from the average normal, and the signs of myocardial involvement were correspondingly less pronounced. Clinically, this case exhibited symptoms of cardiac failure only of short duration.

In one of the cases in the hospital ward, with marked venous stasis, repeated observations were made at intervals of one or more days, extending over a period of six weeks. Following the initial low vital capacity measurement observed on admission of 440 c. c. per sq. m. surface, there was a rapid rise in a period of six days to a value of 1,110 c. c. per sq. m. surface. This rapid rise was coincident with a clearing up of the congestive symptoms. The vital capacity measurements following this initial rise remained more or less stationary tending toward gradual

increase as the patient's clinical condition improved. At the end of six weeks, the vital capacity still showed a reduction of 30 per cent. of the average normal.

The Group with Potential Heart Disease.—The potential group included thirty-five children with no evidence of heart disease, but who had given a definite predisposing history (rheumatism, chorea, etc.). All of these children were found to have a normal exercise tolerance.

The measurements on vital capacity were made on twenty-four girls and eleven boys. Averaging the data together for the boys and girls we obtain the figure 1,876 c. c. per sq. m. surface. The main feature of interest in this value is the similarity it bears to the results obtained in the normal group of subjects. It gives additional corroborative evidence on the functional classification of the potential heart group as one that is normal in all essential respects.

The Significance of Tracheobronchial Adenopathy in the Evaluation of Vital Capacity.—The low vital capacity values obtained in individual subjects of the normal group, and similarly observed in the potential group and in Class 1 suggested investigation as to the possible influence of some pathology of the lung not revealed on physical examination. Fluoroscopic examination of six of the normal subjects with low vital capacity values revealed extensive hilus changes and increased pulmonary markings which were confirmed by roentgenograph. In order to investigate further the possible significance of these findings, a group (A) of thirty-seven normal subjects, and a group (B) of sixty-one subjects from the potential group and Class 1 were arbitrarily selected for comparative fluoroscopic study.[14]

Interpretation of the degree and extent of the hilus shadow and pulmonary markings observed were arbitrarily graded as one plus (denoting little or no evidence of increased hilus shadow and pulmonary markings), two plus (showing definite enlargement of hilus shadow with pulmonary markings extending midway into the lung fields), and as three plus (revealing extensive enlargement of hilus shadow with pulmonary markings extending to the lung periphery). The average vital capacity values were computed for the three grades of Group A and B, respectively.

The average vital capacity values obtained for thirty-seven subjects of Group A were for nine graded as one plus, 2,080 c. c. per sq. m. surface area; for twenty-two graded two plus, 1,690 c. c. per sq. m. surface area, and for six graded as three plus, 1,530 c. c. per sq. m. surface area. The sixty-two subjects of Group B revealed values for

14. These studies were made in the Roentgenological Laboratory of the New York Nursery and Child's Hospital by Dr. I. E. Liss.

eighteen graded as one plus, 2,070 c. c. per sq. m. surface area; for twenty-seven subjects graded as two plus, 1,790 c. c. per sq. m. surface area; and for seventeen graded as three plus, 1,520 c. c. per sq. m. surface area.

A consideration of the combined average vital capacity values of Groups A and B shows for twenty-seven subjects graded as two plus a value of 1,745 c. c. per sq. m. surface area, with individual values high in some instances. Of importance is the value of 1,524 c. c. per sq. m. surface area obtained for twenty-three subjects graded as three plus, with individual values all below the normal standard obtained. Since at the present time the pathology underlying and the significance of tracheobronchcial adenopathy, as observed in children is inconclusive, it is impossible to state whether the reduction of the vital capacity observed in the subjects graded as three plus is a direct mechanical one, or an indirect constitutional one, or merely coincidental.

We have included for comparative study observations made on a group of thirty-two subjects with recurrent bronchitis, asthma, pleurisy, pneumonia and tuberculosis. Roentgenologic study and vital capacity measurements of this group show that ten of the subjects with bronchitis and asthma, having hilus changes graded as two plus, revealed an average vital capacity value of 1,880 c. c. per sq. m. surface area. Thirteen with a similar history graded as three plus gave an average vital capacity value of 1,460 c. c. per sq. m. surface area. The nine subjects having parenchymal and pleural lung involvement revealed an average vital capacity value of 1,220 c. c. per sq. m. surface area, which was in accord with the clinical history and physical examination.

Of interest are the consistent low values obtained in a total of thirty-six children graded as three plus. These observations warrant further investigation which we have undertaken.[15]

DISCUSSION

A study of the relation between the vital capacity in children with heart disease, and the exercise tolerance of these subjects, may be conveniently arranged under three general considerations: First, the vital capacity of the average normal child as a basis for comparison; second, the degree of difference exhibited in the different cardiac classes; and third, the extent to which lung involvement and certain intrathoracic conditions vitiate the vital capacity measurements.

A comparison of several dffierent methods of expressing vital capacity in a relative way indicated that the one relating the vital

15. We have since observed a well developed boy, 13 years of age, with an aortic lesion and a normal exercise tolerance to have a vital capacity within normal limits. Roentgenologic study of the lungs, however, showed extensive hilus changes and some parenchymal lung involvement.

capacity to a unit of body surface was generally best adapted to this work. Although the method of relating the lung capacity to a unit of body weight has seemed to possess approximately the same degree of accuracy, other methods of expressing the values, such as those based on stem length and chest circumference measurements, or groupings according to an arbitrarily selected range of body height, have shown no special advantages. The data on normal subjects between the ages of 6 and 16, show that the boys exhibit a vital capacity only 3.5 per cent. above that for the girls. This difference we consider negligible, so as a general practice the observations on boys and girls have been grouped together and expressed as an average value. It is of interest to note in this connection that in the studies made by West,[12] on adults there was a greater sex difference and also higher values per unit surface area than we have obtained on these younger subjects.

Another feature of the observations on normal subjects is exhibited in the marked individual variation of the vital capacity values. This aspect of the results has proved to be one of the most perplexing questions in the study. There is little doubt in our minds that certain of these differences are to be explained by a lack of proper cooperation on the part of some individuals in the performance of the test, but it was soon apparent that not all of the low results could be accounted for in this manner. It was in the search for other causes that our attention was directed to the probable influence of tracheobronchial adenopathy as a possible factor in producing these results. The conclusion is not warranted at present that all our subjects presenting a low vital capacity, and without diminished exercise tolerance, are due to marked tracheobronchial adenopathy, but the data presented above indicate, we believe, that this factor may play a definitely significant rôle.

The observations on the vital capacity of the different cardiac classes, when considered in terms of group averages, show reduced values in those classes with diminished or markedly reduced exercise tolerance. Moreover, the amount of reduction in the vital capacity measurements obtained, bears a relation to the degree of diminution in the exercise tolerance. We wish to emphasize, however, that these conclusions are based on group values, and cannot be taken to apply unreservedly to individual cases. A consideration of the wide range of variation shown in the normal group of subjects supports the view that a low vital capacity, per se, signifies little concerning the cardiac condition. There is little doubt, however, that when other complicating factors, some of which we have quite clearly identified, are excluded, the vital capacity measurement in children may then be considered a very close index of cardiac functioning. While it appears to us, therefore, that a vital capacity determination may not be accepted as a reliable substitute

for an exercise tolerance test as a measure of heart function, the close correlation in the character of the results obtained with these tests in the different cardiac classes supports the view that it forms a valuable adjunct to the methods for evaluating cardiac reserve.

CONCLUSIONS

1. The vital capacity of eighty-five normal children, comprising forty-four boys and forty-one girls, and ranging in age from 6 to 16 years, gave an average of 1,870 c. c. per sq. m. surface area; with the boys showing only a 3.5 per cent. larger value than the girls.

2. A group of thirty-six children showing extensive hilus changes and increased pulmonary markings radiating to the lung periphery revealed a reduction in vital capacity of 20 per cent. below the average for normal subjects.

3. In children with heart disease, eighty-eight with normal exercise tolerance (Class 1) showed an average vital capacity of only 2 per cent. below the average for the normals; thirty-eight with diminished tolerance (Class 2) showed an average vital capacity 26 per cent. below the average for the normals; and, five with cardiac failure (Class 3) showed a vital capacity from 30 to 50 per cent. below the average for normal subjects. The thirty-five children (potential group) with a normal exercise tolerance showed an average vital capacity equal to the average obtained for the normals.

4. Vital capacity measurements show a close relation to the heart functional capacity, as gauged by the exercise tolerance. They cannot be considered quite so reliable an index of diminished capacity for physical activity in children with heart disease because of the wide variation obtained in the normals and the chance of other complicating factors.

STUDIES OF INFANT FEEDING. XIV

CHEMICAL STUDIES OF CERTAIN DRY MILK PRODUCTS USED IN INFANT FEEDING *

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Dry milk powder is becoming quite extensively used for the feeding of infants and in many ways seems to possess advantages over modified milk formulae. The dry powder is packed by the manufacturers in air tight containers and may be kept in these containers over long periods of time without deterioration. There are several products on the market, such as dry whole milk, dry partly skimmed milk, dry skimmed milk, dry whey, and dry modified milk. There are two processes in use for manufacturing dry milk products.

One process consists of spraying the previously condensed milk into a heated chamber through which a strong blast of hot air is passing; the hot air removes the water and the solid part of the milk falls to the bottom of the chamber in the form of a dry powder. In this process the continued heating necessary for the condensing of the milk seems to reduce the antiscorbutic value of the milk.[1]

The other process consists in the rapid drying of the liquid milk on large polished steel cylinders heated above 212 F. and the dry milk as delivered from the drying cylinders is a translucent, dry, cream-white sheet, which is sifted to a fine powder. During the process of drying the milk is heated to a high temperature, necessary for the thorough removal of the water, for a few seconds only, and this time is so short that caramelization of the milk sugar is avoided and destruction of vitamines seems to be reduced to a minimum.[1]

ANALYSES OF DRY MILK PRODUCTS

In Table 1 will be found the results of our analyses of several dry milk products used in infant feeding.

In connection with the figures given in Table 1, the following comments seem called for:

Sample 203, *Klim* (dry whole milk), manufactured by Merrell-Soule Company. It is claimed by the manufacturers of this product that it is made from fresh whole milk containing 3.5 per cent. fat. By using the ratio noticed by Van Slyke which exists between the

* From the Boston Floating Hospital Laboratories.

1. Hart, E. B.; Steinboch, H., and Ellis, N. R.: J. Biol. Chem. **46**:309, 1921.

fat and protein contents of whole milk [2] it is easily established that their product, which contains 27.70 per cent. fat, should have a protein content of 22.70 per cent. if the product is made from whole milk which contained 3.5 per cent. fat, and the higher protein content, 26.08 per cent. indicates a partial removal of fat from the milk before drying.

By the use of the lactose and ash content of their dried milk as a basis of computation it is found that their original milk contained 3.29 per cent. protein; and that a dry milk powder, made from such a milk, and having a protein content of 26.08 per cent. should have a fat content of 34.0 per cent. These facts lead me to believe that the product Klim (dry whole milk) has been made from milk

TABLE 1.—ANALYSES OF DRY MILK PRODUCTS

	Merrell-Soule Company				The Dry Milk Company	Mammala Corporation
Trade name	Klim Dry Whole Milk	Powdered Modified Milk	Klim Dry Skimmed Milk	Sweet Whey Powder	Dryco	Mammala
Laboratory No.	203	202	204	201	250	212
Moisture	3.23	3.67	3.98	3.71	3.42	3.11
Fat	27.70	16.56	00.00	00.00	11.95	11.16
Lactose	36.14	56.90	47.94	75.90	43.36	51.21
Protein	26.08	16.01	33.60	13.21	33.87	25.20
Citric acid	1.42	1.77	1.90	3.18	1.82	1.22
Ash	5.74	6.94	7.98	9.07	6.97	5.80
Chlorin	1.00	1.25	1.20	1.55	1.06	0.95
Phosphorus	0.80	0.75	1.01	0.75	1.04	0.75
Calcium	1.71	1.29	1.91	1.56	1.57	1.44
Magnesium	0.11	0.23	0.15	0.27	0.17	0.11
Sodium	0.81	0.78	0.90	1.01	0.56	0.59
Potassium	1.03	1.73	1.49	2.09	1.48	1.09

which originally contained 4 per cent. fat but which had its fat content reduced to 3.5 per cent. before drying and that the product is not therefore dry whole milk in a strict sense.

The relation between sodium and potassium in fresh whole cow's milk will generally show one part sodium to 2.2 parts potassium. Dry whole milk should contain about 0.55 per cent. sodium and 1.20 per cent. potassium.[3] The amount of sodium in this sample (0.81 per cent.) in connection with no increase in any of the other constituents would indicate the addition of either sodium carbonate or sodium bicarbonate. This addition of carbonate or bicarbonate at once raises the question as to why it has been used. Has it been used to overcome some mechanical difficulty in the process or has it been added to neutralize the acidity of a milk which is not strictly fresh?

2. Van Slyke, L. L., and Publow, C. A.: The Science and Practice of Cheese Making, Orange Judd Co., p. 170, $[(F-3) \times 0.4] + 2.1 =$ per cent. of casein. F = per cent. of fat in milk.

3. Van Slyke, L. L., and Bosworth, A. W.: J. Biol. Chem. **20**:138, 1915.

Sample 202, *Powdered Modified Milk,* manufactured by Merrell-Soule Company. A study of the percentages of protein, chlorine, sodium, potassium and citric acid in this preparation indicates the addition of sodium chlorid and potassium citrate.

Sample 204, *Klim,* Dry skimmed milk, manufactured by the Merrell-Soule Company. The high sodium content indicates the addition of either sodium carbonate or bicarbonate.

Sample 250, *Dryco,* manufactured by the Dry Milk Company. The manufacturers claim that they mix one part whole milk and two parts skimmed milk in the preparation of this product. If this is so, it is evident that part of the fat is lost during the process of drying for such a mixture of whole milk and skimmed milk should give a dry powder with a fat content of about 14 per cent. instead of the 11.95 per cent. found.

TABLE 2.—THEORETICAL CITRIC ACID CONTENT OF DRY MILK PREPARATIONS AS CALCULATED FROM THEIR PROTEIN CONTENT AND THE ACTUAL CITRIC ACID CONTENT FOUND

No.	Theory, per Cent.	Found, per Cent.
203	1.62	1.42
250	2.12	1.82
202	1.00	1.77
212	1.58	1.22
204	2.10	1.90
201	3.30	3.18

Sample 212, *Mammala,* manufactured by the Mammala Corporation. The relation between the sodium and potassium in this sample indicates the addition of a small amount of sodium carbonate or bicarbonate.

CITRIC ACID CONTENT OF DRY MILK PREPARATIONS

Citric acid is one of the constituents of milk which has received very little attention from the standpoint of infant feeding. It is my opinion that the antiscorbutic value possessed by certain foods is in some way connected with their oxy-acid content, and that in milk citric acid is the oxy-acid involved in this connection. Such being the case, it is of interest to note the citric acid content of the dry milk powders, for it is possible by heat to decompose this acid. In Table 2 will be found figures giving the amounts of citric acid found in the preparations examined and the amounts of citric acid they should contain providing the milk from which they were made contained 0.2 per cent. citric acid, the average amount found in fresh cow's milk.

It will be noticed that there seems to be a loss of citric acid in all the products except No. 202, Merrell-Soule Company's Powdered Modified Milk. This loss of citric acid during the drying process deserves further investigation.

In the case of sample 202, Merrell-Soule Company's Powdered Modified Milk, it would appear that this product contains an excess of citric acid, indicating that in the preparation of this powdered milk some citrate has been added. This deduction is strengthened by the high ash content of this preparation in contrast with its low protein content.

CHANGES IN THE SOLUBILITY OF SOME OF THE MINERAL ELEMENTS IN MILK AS THE RESULT OF DRYING

During the process of drying, a degree of heat is used which brings about a change in the chemical arrangement of some of the constituents. This is shown by the figures given in Table 3. In line 1 will be found the percentages of the different mineral constituents in fresh whole milk which are in true solution and they should be compared with the percentages given in the other lines in order to show the changes in solubility produced by drying.

TABLE 3.—DEGREE OF SOLUBILITY OF SOME OF THE MINERAL ELEMENTS IN MILK AND DRY MILK PRODUCTS

	Lab. No.	Chlorin	Phosphorus	Calcium	Magnesium	Sodium	Potassium
Fresh cow's milk.....	...	100.00	53.60	33.33	53.85	100.00	100.00
Klim, dry whole milk.....	203	100.00	22.58	35.83	100.0	100.00	100.00
Powdered modified milk...	202	100.00	54.38	60.00	100.0	100.00	100.00
Klim, dry skimmed milk...	204	100.00	25.54	51.68	92.0	100.00	100.00
Sweet whey powder.....	201	100.00	64.32	52.05	75.55	100.00	100.00
Dryco.....	250	100.00	36.62	14.90	15.00	100.00	100.00
Mammala.....	212	100.00	36.62	80.69	94.44	100.00	100.00

In connection with the above figures it is of interest to note the percentages of soluble calcium in the different products. In fresh cow's milk 33.33 per cent. of the total calcium is soluble and the dry milk products, with the exception of No. 250, all show an increase in the percentage of soluble calcium. This change in the solubility is an important factor to be considered in connection with the use of these dry milk preparations for infant feeding. Cow's milk, when used as a food for infants, contains an excessive amount of available [4] calcium and it is this available calcium which is responsible for the soapy stools [5] and protein curds [6] eliminated by most bottle fed infants. From this standpoint, therefore, any method or process which reduces the soluble and available calcium in cow's milk is a very desirable attainment.

4. Bosworth, A. W.: Ann. Med. **1**: No. 4, 1921.

5. Bosworth, A. W.; Bowditch, H. I., and Giblin, L. A.: Am. J. Dis. Child. **15**:397 (May) 1918.

6. Bosworth, A. W.: Am. J. Dis. Child. **22**:193 (August) 1921, and a paper soon to appear in the same journal, "The Calcium of Cow's Milk in Its Relation to Digestion and Absorption of Casein. Protein Curds in Stools."

A CLINICAL AND RADIOGRAPHIC STUDY OF THE THYMUS IN INFANTS*

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For many years hyperplasia of the thymus, either alone or in association with hyperplasia of other lymphoid structures, has been considered as a cause of sudden death in infants and children and as the underlying factor in the production of certain clinical manifestations spoken of as "thymic asthma."

In the literature many theories are found, not only regarding the function of the thymus, but regarding the mechanism by which an enlarged thymus induces dyspnea, cyanosis, stridor, convulsions and death. Whether the symptoms are produced as the result of a specific substance elaborated by the thymus gland, whether they are caused by a gland deficient in specific substances, or whether they are brought about by compression of the trachea, nerves or great vessels remains at the present time unsettled. However, real progress has been made in the recognition of the condition and a satisfactory treatment has been established for its relief. In 1904 Dr. Friedlander,[1] having in mind the studies by Heineke [2] who demonstrated the effects of the roentgen ray on lymphoid tissue, suggested this form of treatment in an infant suffering from severe suffocative attacks, due to an enlarged thymus. This was the first patient successfully treated with the roentgen ray. In following years numerous reports have been published, not only by Friedlander, Lange [3] and their co-workers, but by workers in all sections of this country and abroad. The roentgen-ray diagnosis and therapy now is a well established fact.

While the average normal weight of the thymus is variable, a gland weighing more than 15 gm. is regarded as being pathologic. It is difficult to determine whether or not the thymus is enlarged by the weight of the thymic tissues alone. This is nicely shown by the careful investigation of Hammar.[4] He estimated the exact amount of

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* From the Pediatric and Roentgen-Ray Department of the College of Medicine, University of Cincinnati and the Cincinnati General Hospital.

1. Friedlander: Diagnosis and Treatment of Enlarged Thymus, Am. J. Dis. Child. **6**:38 (July) 1913.

2. Heineke: Ueber die Einwirkung der Röntgenstrahlen auf Tiere, München. med. Wchnschr. **50**:2090, 1903.

3. Lange: The Present Status of the Roentgen-Ray Therapy of Enlarged Thymus. Am. J. Roentgenol. **1**:74, 1913.

4. Hammar: Thymus Histology in So-Called "Mors Thymica," Svenska Läkares. Handl. **42**:867, 1916. (Quoted from Endocrinology **1**:88, 1917.)

parenchyma minus the fat and connective tissues and counted the number of Hassals' corpuscles. In only two of thirteen cases of thymus death was the thymus enlarged.

In view of the opinions which are held as to what constitutes an enlargement and with the increasing use of the roentgen ray in the diagnosis and treatment of enlarged thymus, additional data bearing on this subject is of interest. In this report we shall present the results of our observations in a patient who died suddenly with the symptoms of an enlarged thymus together with the study of infants who presented no symptoms referable to this gland.

In one patient we determined by percussion and by roentgenogram the size of the thymus during life and compared them with the thymus gland in situ, after death.

REPORT OF CASE

History. — An infant, 4 months of age, weighing 11 pounds, was born at term. The delivery was normal. He was a large well-nourished breast-fed infant. No abnormalities were noted on examination. There were no evidences of rickets or tetany. The Wassermann and von Pirquet tests were negative.

On the second evening after admission the patient had a convulsive attack accompanied by cyanosis and inspiratory stridor. An enlargement of the thymus was suspected as there was dulness 1 inch to the right and 1¼ inches to the left of the midsternal line. Below the second interspace the dulness was continuous with the cardiac dulness. This diagnosis was confirmed by the radiogram and the routine roentgen-ray treatment was given at once. After the patient was returned to the ward, he did not seem to be in an alarming condition although some dyspnea and cyanosis continued. Two hours after the roentgen-ray treatment and three hours after the initial symptoms, he died suddenly.

At necropsy, the thymus, which was apparently enlarged, weighed 17 gm. It extended from the upper level of the clavicle, downward to within half an inch of the lower border of the heart. The heart was almost completely enclosed, anteriorly and laterally by the enlarged gland. The superficial and deep lymph glands, Peyer's patches, the solitary follicles and other lymphoid tissues were not hyperplastic. The spleen which weighed 13 gm. was not enlarged. There were no evidences of compression of the trachea, or of abnormality of the great vessels in this region. The pathological examination other than the enlarged thymus revealed nothing abnormal. Microscopically, the thymus showed no characteristic findings.

Before opening the thorax the thymus was percussed with the body in various postures. Dulness was determined most definitely and readily with the body in the horizontal position. The head resting on the occiput and in semiflexion, the arms extended and clasped about the head, and the legs slightly flexed. The head and vertebral column were held in the medium position. Any deviation from this position, as for instance forcibly turning the head to one or the other side, caused a variation in the percussion note. The most marked change in dulness was produced by altering the position of the head. The dulness obtained with the head in semiflexion, disappeared completely

on extreme dorsal flexion of the head. As Park [5] has pointed out, this change on percussion does not depend upon the upward and downward movement of the thymus but rather on the increase in the antero-posterior diameter of the chest. There was an increase in the antero-posterior dimension of the thorax in the patient at the sterno clavicular articulation of nearly one-eighth of an inch when the head was in extreme dorsal flexion.

Before death, as mentioned above, the dulness on percussion extended from the level of the clavicle, in almost a straight line down to the second interspace—one inch to the right and one and a quarter inches to the left of the midsternal line. The dulness was continuous with the cardiac dulness below this point. This area of dulness when compared with the shadow cast by the roentgen ray was identical (Fig. 1). The percussion dulness as obtained after death, corresponded closely to that during life. We feel the clinical symptoms could not

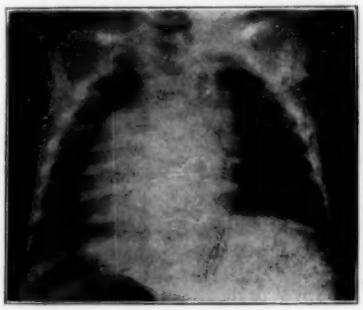

Fig. 1.—Roentgenogram taken before death. Compare the shadow with the location of the thymus in Figure 2.

have been produced by the thymus becoming suddenly enlarged by venous engorgement—a theory which has been offered to explain the sudden onset of symptoms in an apparently normal infant—as the difference between the shadow cast before death and that cast after death was so slight.

At necropsy, the thymus actually filled the anterior mediastinum (Fig. 2) and its location agreed in every particular with the dulness which was obtained on percussion and with the shadow in the roentgen ray. The greatest increase in width of the thymus in the transverse diameter was in the second interspace. Anatomically the thymus completely overlaid the upper part of the heart and as shown in the roentgen ray overshadowed its normal outline and angles. These com-

5. Park: Criticism of Two Percussion Methods for Diagnosis of Enlarged Thymus, Arch. Int. Med. **10**:214, 1912.

parative studies show definitely that a thymus weighing seventeen grams can be made out readily by percussion and that it casts a characteristic shadow in the roentgen ray.[6]

Sixty patients without symptoms referable to the thymus were examined with particular reference to percussion dulness and to the roentgen-ray shadow of the thymus. The patients varied in age between 5 hours and 1 year. Thirty-five of the patients were 2 weeks of age, ten were between 1 and 4 months old, ten were between 4 and 8 months old, and five were from 8 to 12 months of age. The patients under 1 month were, for the most part, normal breast-fed infants born in the hospital. The other patients were being either breast-fed or artificially fed.

The following routine examination was made: The patient was placed on a firm table, the arms were clasped about the head which

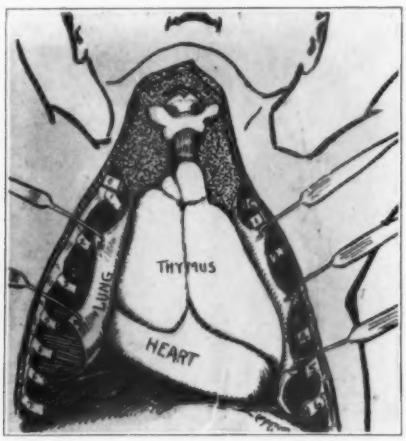

Fig. 2.—Sketch made by Dr. Maytum of thymus in situ. Compare with shadow in Figure 1.

was held in semiflexion and the body maintained in the median position by an attendant. The slightest possible stroke should be used in percussing for thymic dulness. Indeed, we are convinced that the dulness can be more accurately determined by the tactile sense of resistance than by sound. Having accurately indicated the midsternal line, percussion was made starting at the extreme edge, over the left and then the right side of the upper part of the thorax. A change in percussion was noted and measured. The routine roentgen-ray examination was made as follows: The same position as mentioned above was main-

6. In the following discussion other factors, such as new growths, enlarged glands, malformations of the heart, etc., which cast shadows in this region have been excluded.

tained. The ray was centered over the level of the upper border of the first rib. A universal Coolidge tube was used with 40 ma., a rather high voltage, 65 kilowatts—practically a six inch spark gap. The exposure, from one-sixtieth to one-thirtieth of a second, was made at a distance of twenty-four inches. The picture was taken on plates made with a single screen. Repeated trials are often necessary in order to obtain a picture which is accurately "centered," that is an equal distance from the midline of the spine to the right and left axillary border. Any deviation from this position, such as tilting to one side or the other, produces an asymetry of the two halves of the chest with a dis-

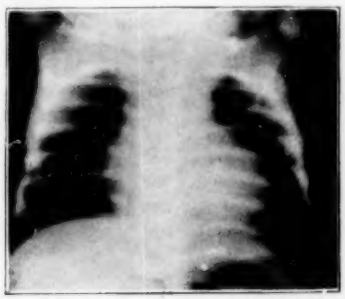

Fig. 3.—Roentgenogram taken with patient maintained in standard position. Note shadow to left and right of midline in second interspace. Compare with Figure 4.

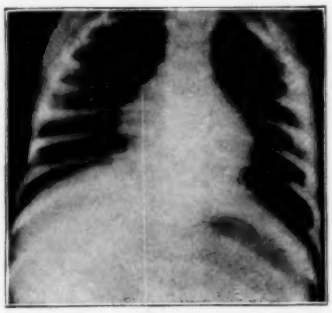

Fig. 4.—To show effect of position. Head maintained in extreme dorsal flexion. Note disappearance of shadow seen in Figure 3.

placement of the heart and great vessels. Correct position and technic is essential in making a roentgenogram to demonstrate the thymus. We have found that the thymic shadow may appear either to one side or the other by incorrectly centering the central ray or by failure to place and maintain the patient in the exact center of the plate. When the head is held in extreme dorsal flexion the thymic shadow cast in the radiogram becomes greatly diminished in size or it may entirely

disappear (Figs. 3 and 4). We believe that the shadow cast by the thymus remains the same whether the radiogram is taken at the end of inspiration or expiration. In this series, they were taken at the end of inspiration.

The presence or absence of dulness in the second interspace to the right and left of the midsternal line was used to differentiate between a "negative" and a "positive" thymus. We took this as our criterion as in the patient studied at necropsy the transverse diameter of the thymus was greatest at this point. We regarded the thymus as "negative" if dulness extended not over seven-eighths of an inch to the

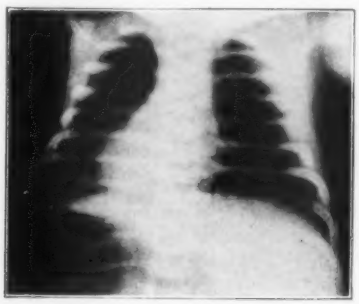

Fig. 5.—Normal infant. Note absence of shadow to right and left of midline. Negative thymus.

Fig. 6.—Normal infant. Note absence of shadow to right and left of midline. Negative thymus.

left and if there was no dulness, or if it was not over half an inch to the right of this point. Dulness in the second interspace both to the right and to the left of the midsternal line and continuous with the cardiac dulness below was regarded as a "positive" thymus. Disappearance of dulness with the head in extreme dorsal flexion, was confirming evidence. The roentgen ray differentiation between a negative and a positive thymus was made according to the extent of the shadow cast

to the right and left of the mid line. In the "positive" thymus, the shadow in the anterior mediastinum was either continuous with the heart shadow, obliterating the normal cardiac angles, or it was superimposed on the heart shadow as a broad cap.

The results of the two studies were as follows: Thirty-one of the sixty patients failed to show a shadow in the anterior mediastinum, indicative of the thymus (Figs. 5 and 6). Twenty-nine of them showed a shadow which, according to the roentgen-ray interpretation, was indicative of thymus (Figs. 7 and 8). A comparison of the roentgen-ray findings and the physical findings show that twenty-seven patients were

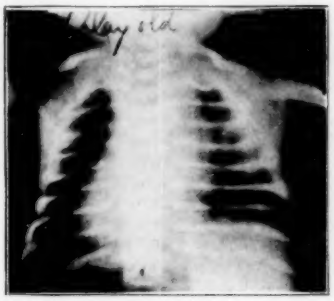

Fig. 7.—Normal infant. Note shadow to the left and right of midline continuous with heart shadow. Positive thymus.

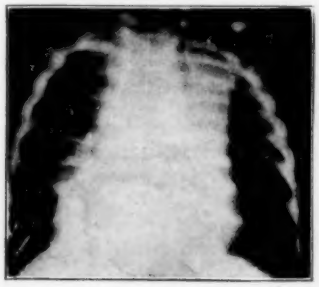

Fig. 8.—Normal infant. Note shadow to left and right of midline continuous with heart shadow. Positive thymus.

negative both with the roentgen ray and on percussion; twenty patients were positive both with the roentgen ray and on percussion; four patients were negative with the roentgen ray and positive on percussion; nine patients were positive with the roentgen ray and negative on percussion. As might be expected in the interpretation of slight changes by percussion, dulness was detected in a few patients in which no confirming shadow was found by the roentgen ray. In other

patients the roentgen ray picture showed a shadow in the anterior mediastinum which was not detected on percussion. One patient illustrates with what care changes on percussion must be interpreted. The clinical note reads, "No dulness to the right or left of the midsternal line in the second interspace." The roentgen ray report says, "There is a shadow completely filling the mediastinum and extending in the right and left to the axillary border." The misinterpretation of the percussion sound in this patient was due to the fact that there was not a sufficient area of normal resonance present to detect the change between the normal resonance and the dulness.

The infants were not suffering from any of the clinical symptoms which are said to be characteristic of a patient with an enlarged thymus. The majority of them were normal infants, or they were in the hospital being treated for nutritional disturbances, hereditary lues, hypertrophic stenosis of the pylorus, acute otitis media, genococcus vaginitis, etc. There was no relationship so far as we could ascertain between the state of nutrition, specific diseases or infections and the shadow cast in the roentgen ray. Evidences of hyperplasia of lymphoid tissues were sought for, such as enlargement of the tonsils, of the superficial lymph glands and of the spleen but they were not constant features of the patients with positive findings. As goiter is a frequent manifestation in the territory in which these observations were made, an attempt was made to find out the prevalence of goiter among the mothers of the patients. It was an inconstant finding. While the thyroid gland was distinctly palpable in many of the patients we are inclined to believe it bore no relationship to the enlarged thymus. Indeed, in one patient, an infant, 2 weeks old, who had a congenital goiter, there was no shadow in the anterior mediastinum. The proportion between the positive and negative cases was not influenced by the age of the patient nor by the state of nutrition. A large well-nourished infant, 5 hours old, showed a negative thymus, whereas in an undernourished baby of 7 months, weighing 8 pounds, the shadow was as large as any of those we have seen in the roentgenogram of patients with definite clinical symptoms.

The total number of leukocytes and the differential count of the blood in six of the infants with positive findings failed to show any abnormality which might be said to be characteristic of a generalized hyperplasia of the lymphoid structures.

In this series of sixty infants, twenty-nine of them, or about 50 per cent., showed a shadow in the anterior mediastinum by roentgen ray. In twenty of the twenty-nine patients dulness was found on percussion. The percussion changes and the radiograms corresponded with those which have been described by other workers as being characteristic of

an enlarged thymus. They agreed with those found in the patient with symptoms of thymic asthma, in which the thymus weighed seventeen grams.

In order to determine that the shadow in the anterior mediastinum was caused by the thymus, we exposed a small number of infants to the roentgen ray. Each patient was given one routine treatment.[7] At the end of one week, a second roentgenogram was taken. In all of the patients so treated there was a distinct diminution in the size of the shadow after this procedure. Roentgenograms taken after a week in a small number of patients untreated showed a persistence of the shadow. Several of the patients were reexamined also after a period of several weeks and the shadow was still present.

Blood Count in Six Positive Cases

Case No.	Leukocytes	Polymorph., Per Cent.	Lymphocytes, Per Cent.
30	10,800	30	68
21	10,400	42	50
24	10,000	37	62
20	12,500	34	59
22	9,800	40	58
8	11,500	32	64

During the course of this study we saw six infants who presented clinical symptoms of an enlarged thymus and on percussion there was an increased dulness to the right and left of the midsternal line in the second interspace and which was continuous with the cardiac dulness. In each patient the roentgenogram revealed a shadow in the anterior mediastinum indicative of an enlarged thymus. After the routine roentgen-ray treatment there was an improvement in the clinical symptoms and the shadow disappeared. A brief abstract of the history of two of these patients is given:

Case 1 (19).—*History.*—E. Z., aged 2 months; breast-fed; was regarded previous to the present illness as a normal infant. When 5 weeks old she had a generalized convulsion which lasted a few moments. From then on she had difficulty in breathing and had frequent attacks of cyanosis. On one occasion the baby was found in the bed, unconscious, the face gray and the eyelids purple in color, and gasping for breath. Three weeks after the initial attack, the baby was brought to the hospital.

Examination.—The baby was undernourished and weighed 7½ pounds. The temperature was normal. There was present a marked inspiratory stridor and a hoarse brassy cough. This was increased by crying. There was no cyanosis.

7. The treatment was as follows: Exposure with central ray is made directly over the middle portion of the thymic region anteriorly and posteriorly, for five minutes each, with a 9-inch spark gap—5 ma, 9-inch distance with 3 mm. aluminum and sole leather filter.

On percussion there was dulness in the second interspace 1 inch to the left and three-fourths inch to the right of the midsternal line. Below the dulness was continuous with the cardiac dulness. The examination otherwise was normal. The superficial lymph glands and the spleen were not enlarged. There was no evidence of rickets or tetany.

The leukocytes numbered 8,600. The roentgen ray showed a shadow in the anterior mediastinum extending well to the right and left of the midsternal line in the second interspace and being continuous with the left border of the heart.

Clinical Course.—After three roentgen-ray treatments at weekly intervals the roentgen-ray picture showed that the shadow had disappeared. When seen after the third treatment there was no inspiratory stridor and the respirations were normal, and no cyanosis was observed when crying. The mother stated that the difficulty in breathing lessened after the first treatment.

CASE 2 (20).—*History.*—Baby Reis, aged 4 months; breast-fed. Since birth it had been noticed that there was difficulty in breathing. At times there was an inspiratory crow and the breathing was so loud it could be heard "on the street." Often when nursing or crying the baby would have such a severe paroxysm that it would become "blue in the face" and the mother thought the baby was dying. A brother who died in convulsions at 14 months of age presented similar symptoms from birth.

Examination.—The baby was well nourished and appeared normal, except for a wheezy inspiratory and expiratory dyspnea. The voice was normal but on coughing a loud whistling inspiratory sound was heard. At times the cough sounded exactly like that produced by an aneurysm of the aorta. Percussion revealed dulness in the second interspace, extending 1¼ inches to the left and 1⅛ inches to the right of the midsternal line and was continuous with the cardiac dulness below. Otherwise the physical examination was negative.

The leukocytes numbered 12,200; the polymorphonuclear neutrophils were 41 per cent., the lymphocytes 60 per cent. The roentgen ray showed a shadow in the anterior mediastinum which corresponded exactly with that on percussion. The superficial lymph glands and the spleen were not enlarged. There was no evidence of rickets or tetany.

Clinical Course.—There was marked improvement in the clinical symptoms, and after two roentgen-ray treatments the shadow was greatly diminished. The patient has not returned for further observations.

We have been unable to find any points of differentiation between the roentgen-ray shadow found in patients with the clinical symptoms of enlarged thymus and the thymus shadow in "normal" infants. Dr. Little, in an analysis of over two hundred roentgen-ray pictures of infants referred to the Roentgen-ray Department of the Cincinnati General Hospital with the clinical diagnosis of enlarged thymus, failed to find a difference between them and the roentgen-ray shadow cast in the "normal" infants of our series. These patients were given three treatments at ten day intervals (Figs. 9 and 10). The majority of them received prompt relief. Six required a second series of treatment. The roentgenogram taken at the conclusion of the treatment showed a much smaller shadow in all cases than at the beginning of treatment. We believe that a shadow in the anterior mediastinum which does not diminish in size after intensive roentgen-ray therapy is not the shadow of the thymus.

Just how difficult it may be to differentiate between an enlarged thymus causing symptoms and a thymus sufficiently large to cast a shadow but in which symptoms are not due to the thymus is shown by the following case report:

CASE 3.—*History.*—A colored female infant weighed 6 pounds at birth. Immediately following delivery it was observed that there was difficulty in breathing. There was marked inspiratory stridor and cyanosis. The dyspnea was constant and from time to time it became paroxysmal; being increased by crying and nursing. The paroxysms would begin with a series of inspiratory efforts followed by a loud crowing inspiratory sound and then followed by a short

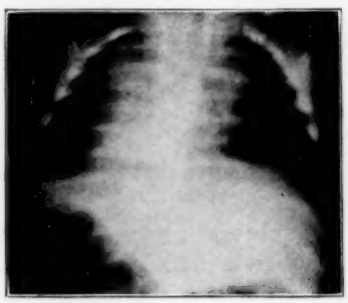

Fig. 9.—Age, 3 months. Cyanosis, inspiratory dyspnea and convulsions before roentgen-ray treatment.

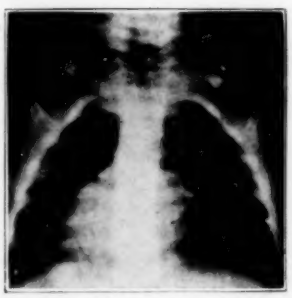

Fig. 10.—Roentgenogram after three roentgen-ray treatments, ten day intervals. Note complete disappearance of shadow shown in Figure 9.

expiratory effort. During this, there was marked retraction of the supraclavicular and infraclavicular spaces and the intercostal spaces. There was an anxious expression of the infant, the eyeballs became prominent and there was extreme cyanosis. On several occasions the attacks were so severe as to require artificial respiration.

Physical Examination.—Negative, except for an area of increased dulness in the region of the thymus. The dulness extended 1¼ inches to the left and seven-eighths inch to the right of the midsternal line. It was continuous below with the cardiac dulness. This area of dulness disappeared when the infant's head was held in extreme dorsal flexion. It was also noticed that the symptoms were markedly relieved when this position was assumed. It was repeatedly observed that the symptoms could be induced and relieved by the position

of the infant's head. When first seen it was believed from the increased area of dulness that the symptoms were due to an enlarged thymus. The possibility of congenital malformation of the larynx was however considered.

Clinical Course.—Inasmuch as the roentgenogram showed a shadow in the upper mediastinum indicative of an enlarged thymus, a series of roentgen-ray treatments were begun. Although no marked improvement in the symptoms followed this treatment the shadow in the roentgenogram entirely disappeared. Inasmuch as the infant was being breast-fed and the paroxysms were less frequent, the patient was discharged after one month. Ten days later the patient was brought to the dispensary in a severe attack which was relieved after artificial respiration and stimulation.

An examination with the laryngoscope showed an infolding of the epiglottis with each inspiration. This was considered sufficient to explain the symptoms. However, as the roentgen ray showed an indefinite shadow in the anterior mediastinum, a second series of treatments were given. After three weeks there was no marked improvement in the symptoms. We believe that this patient suffered from congenital laryngeal stridor and that the thymus although sufficiently large to be detected by percussion and to cast a shadow by the roentgen ray was not the underlying factor.

When the question arises as to whether the symptoms are due to the enlarged thymus or to some other condition, the patient should be given the benefit of the doubt and roentgen-ray treatment administered.

We feel reasonably certain that the roentgen-ray shadow in this group of normal infants is due to the thymus as it disappeared after exposure to the roentgen-ray; it could not be distinguished from the shadow which at necropsy was proven to be cast by the thymus, and it is identical with that found in patients with clinical evidences of an enlargement of the thymus. Whether this should be interpreted as an enlarged thymus or whether it should be regarded as normally occurring in a certain percentage of normal infants cannot be stated at the present time.

THE SIZE OF THE INFANTILE PALATE*

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It is accepted among those interested in orthodontia that congenital, hereditary and also acquired conditions are factors in the etiology of malocclusion and mouth breathing. The former are at present beyond our control. However, certain of the acquired conditions, ricketts, local dental lesions, malnutrition, and adenoids, can be controlled by preventive and curative measures. Adenoids, in particular, have been blamed for a very large proportion of those suffering from misshapen jaws. It is not yet known in what manner and how early in the child's development these acquired conditions produce their effects, and such data are essential to a rational effort at preventive therapy.

The scope of the work as originally planned involved a study of rachitic infants, infants with large tonsils and adenoids, mouth breathers, and a comparison of these palates with the palates of normal children. It was found that no satisfactory measurements of the infantile palate had been made on the living subject and it was decided first to fill this hiatus. Unfortunately other duties have prevented and probably will prevent the completion of this rather comprehensive plan. However, the preliminary work on the infantile palate has been finished and it seemed worth while to record this fragment; at least it has demonstrated a satisfactory method of measuring the palate and indicates a fruitful line of attack on the problem as a whole.

The only measurements of the infantile palate that could be found in the literature are those of Alkan,[1] who examined the palates of thirty-six new-born infants. The method of mensuration used by Alkan seems rather crude and the criteria of the shape and size of the palate appear ill chosen. The width was obtained by placing the arms of a compass on the alveolar margins, removing the compass from the mouth and measuring the spread of the compass on the straight rule. "The width of the palate was measured in only one place, which corresponded to about the mid-point on the alveolar arch." Alkan himself referred to the greater accuracy of plaster casts; indeed it must be quite impossible to determine exactly the mid-point on a tiny infant's arch, even if the mechanical difficulties of manipulating

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* From the Children's Service of the New York Nursery and Child's Hospital, and the Department of Pediatrics, Cornell University Medical College.

1. Alkan: Arch. f. Laryngol. u. Rhinol. **10**:441, 1900.

infant and compass are overcome. Furthermore, the reasons are not clear for choosing this part of the alveolar arch. The mid-portion of the alveolar arch does not correspond to any fixed anatomical point (as does the position of the molars or the pre-molars in the second dentition) nor does it represent an absolute value, such as the greatest width or the greatest height. Alkan measured the height of the palate indirectly by constructing a triangle, measuring from either alveolar margin to the median raphé. Thus from the three sides of the triangle he calculated the height of the palate by measuring the line dropped from the apex of the triangle (the raphé) to the base line (the width of the alveolar arch) (Fig. 1). This technic involves the removal of the compass from the mouth in measuring each side of the triangle. It is difficult to conceive how, in measuring the two sides of the triangle, one could find the same points on the alveolar margin and the raphé, a procedure which accurate mensuration demands.

The two prerequisites to determining the size and shape of the infantile palate are first, an accurate method of mensuration and second, fixed standards for estimating the size of the palate.

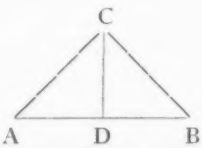

Fig. 1.—Alkan's method of measuring height of palate: A-B, width of palate; A-C and B-C, distance from alveolar margin to raphe; C-D, height of palate.

For the technic of measuring the palate I am indebted to Dr. Frederic L. Stanton. This method involves two procedures, making a model in plaster and measuring the cast with the surveying apparatus of Dr. Stanton. The smallest size plate is cut down to conform to the infant's mouth and a wax impression is made in the manner employed by dentists. From the impression a plaster or rather a dental stone cast is poured, and from this, measurements are taken. Mensuration was done with the surveying apparatus used by Dr. Stanton in orthodontic work (Fig. 2). Only the principles on which the instrument works will be mentioned here; the details of its application have been discussed elsewhere.[2] The surveying apparatus projects to full scale all the dimensions of the cast to be measured. Thus in the cast we have a permanent reduplication of the infant's palate and from this, with the help of the surveying apparatus, one may analyze its

2. Stanton, F. L.: Dental Digest, 1917. Fish, G. D.: Internat. J. Orthodont. **3**: (June) 1917. Stanton, F. L. and Hanan, R. L.: Proceedings of Panama Pacific Dental Congress, September, 1915.

contour, measure the greatest width or the width at the mid-point, the greatest height or the height at any distance from the frenum, the shape of the alveolar arch, and so forth (Fig. 3).

The criteria adopted for estimating the shape of the palate were the greatest width and the greatest height. The greatest height was chosen because the high palate is one of the supposedly characteristic features associated with changes due to malocclusion and mouth breathing in older children, and this measurement would serve as a basis for comparison. The greatest width was chosen rather than the width at

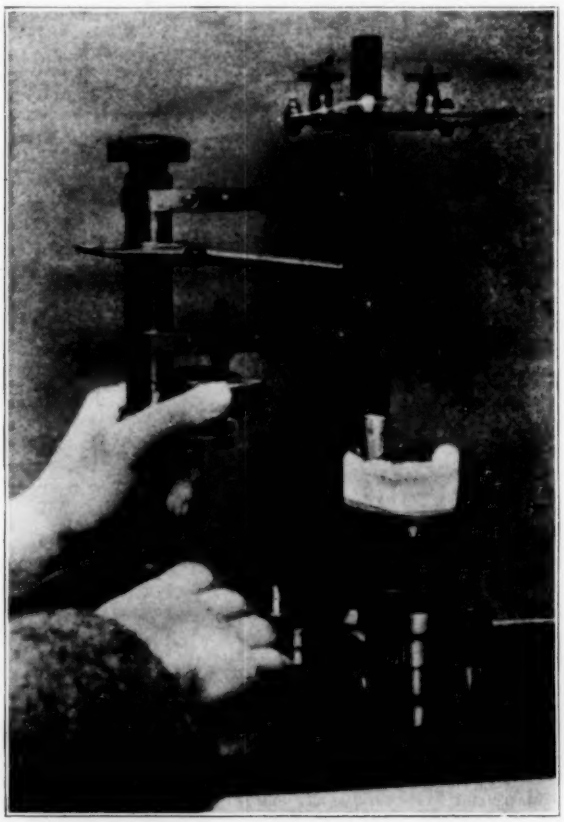

Fig. 2.—Dr. Stanton's surveying apparatus.

any fixed distance from the frenum because there are no anatomical landmarks on the infant's jaw that bear any logical relationship to the height or the later development of the palate. Furthermore, the greatest width like the greatest height is an absolute and not a relative figure. It is customary for purposes of comparison to express the relationship of height to width by the index $\frac{\text{Height}}{\text{Width}} \times 100$, and this formula has been followed.

TABLE 1.—Average Dimensions of Palates of Children Under 1 Year

Number of Cases	Greatest Width (Average), Mm.	Greatest Height (Average), Mm.	$\frac{\text{Height}}{\text{Width}}$ index (Average)
39	30.9	8.79	28

TABLE 2.—Dimensions of Palates of All Children Studied

Age	Case Number	Weight	Greatest Width	Greatest Height	$\frac{\text{Height}}{\text{Width}}$ index
3 months	12	$8^{10}/_{16}$	32.5	8.7	27
4 weeks	29	$6^{10}/_{16}$	27.5	8	29
4 weeks	25	6	29	8	27
12 days	10	$8^{12}/_{16}$	30	11.3	37
6 weeks	30	$5^{10}/_{16}$	28.5	8	28
6 weeks	31	6	30	9.9	33
6 weeks	22	$9^{8}/_{16}$	30.5	9.6	34
7 weeks	14	$6^{10}/_{16}$	28	7.4	26
2 months	13	7	28	9.5	34
2 months	41	14	27	7.7	28
2 months	23	$8^{10}/_{16}$	31	10.1	33
2 months	19	$4^{8}/_{16}$	28.5	7.5	26
3 months	9	.....	32	7.4	33
3 months	12	$8^{10}/_{16}$	32.5	8.7	27
4 months	8	11	33	9.7	29
4 months	16	12	32	9.4	29
4 months	21	9	30	8.7	29
4 months	7	11	34	9.5	28
4 months	3	$10^{2}/_{16}$	32.5	10	31
5 months	43	9	32	8.2	26
5 months	44	10	30.5	10	33
5 months	4	$9^{8}/_{16}$	30	8.6	28
5 months	5	$12^{8}/_{16}$	28.5	9	32
6 months	34	$9^{6}/_{16}$	31.5	9.6	30
6 months	36	11	30.5	8.6	28
6 months	35	7	28.5	7.2	26
7 months	15	$8^{6}/_{16}$	31.5	7.7	24
7 months	6	9	30	8.7	29
7 months	33	10	32	8.1	29
8 months	42	$17^{12}/_{16}$	33.5	8.3	25
8 months	45	9	31.5	9.9	25
9 months	28	17	35	8	34
9 months	38	14	32.5	7.1	23
10 months	37	19	36	9.3	23
11 months	26	$12^{10}/_{16}$	30	9.5	26
11 months	40	17	34	9.4	28
11 months	39	13	33	8.1	25

TABLE 3.—Average Dimensions at Different Ages

Age	Number of Cases	Greatest Width (Average), Mm.	Greatest Height (Average), Mm.	$\frac{\text{Height}}{\text{Width}}$ index (Average)
1 to 3 months, inclusive	13	29.4	8.7	28
4 to 6 months, inclusive	12	31	9	29
7 to 11 months, inclusive	11	32.6	8.5	26
	39*	30.9*	8.79*	28*

* Average dimensions in children under 1 year.

TABLE 4.—Average Palatal Measurements of Children Classified According to Weight

Weight	Number of Cases	Greatest Width (Av.), Mm.	Greatest Height (Av.), Mm.	$\frac{\text{Height}}{\text{Width}}$ index
Under 10 pounds*	19	29.9	8.7	29
Ten pounds and over†	15	32.5	8.9	27

* Average age 3½ months. † Average age 6⅔ months.

Thirty-nine children under 1 year of age were studied. Most of the cases were taken from the "feeding" service of the New York Nursery and Child's Hospital—a ward in which ill nourished infants, foundlings and infants awaiting adoption are cared for. Thus, although a few showed normal weights, most of the infants were under weight; many were mildly rachitic but none severely so.

Table 1 gives the average for all the cases. The greatest width is 30.9 mm. and the greatest height, 8.79 mm. The $\frac{\text{Width}}{\text{Height}}$ index is 28. Table 2 tabulates the findings in all cases. Table 3 indicates that the variations according to age fall within narrow limits. The average palate of the infant from 6 to 12 months of age is a little broader, but no higher than that of the one month old baby. The palate of the heavier child bears a similar relationship to that of the lighter (Table 4), but it is impossible to determine whether this difference is due to increasing age or weight.

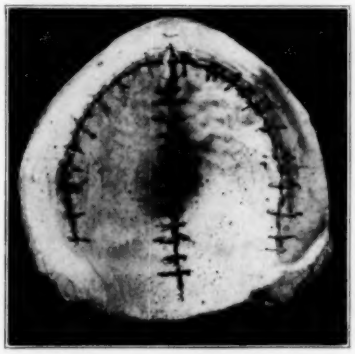

Fig. 3.—Dental stone cast of palate. The points surveyed have been made heavier to permit photographic reproduction.

It would be futile to compare these measurements with those of Alkan for reasons already indicated—the difference in technic and the fact that Alkan measured not the greatest width and the greatest height but the width and height at the mid-point of the alveolar arch. The normal $\frac{\text{Width}}{\text{Height}}$ index for adults according to Bloch [3] falls between 44 and 58; that is to say, the infant's palate is broad and flat and the adult's is comparatively high and narrow.

SUMMARY AND CONCLUSIONS

It has been stated that failure to remove hypertrophied adenoids before the sixth month, "leads to the development during the first year of the short upper lip, the narrow high vault . . . which are associated with the adenoid face" [4] and it is the general impression that other acquired conditions affect the shape of the child's jaws and teeth early

3. Bloch: Verhandl. d. Deutsch. Otol. Gesellschaft **9**:11, 1902.
4. Freeman: New York State M. J. **21**:50 (Feb.) 1921.

in life. These observations may be quite correct, but accurate data to support them are at present lacking. Those in charge of child caring institutions, where the children remain under observation for a long period of time, have the opportunity of making valuable contributions to our knowledge of the changing shape of the jaw and the effect of large tonsils and adenoids, ricketts, bottle feeding and the like, on the development of the palate and neighboring structures. The present work establishes the greatest width (30.9 mm.), the greatest height (8.79 mm.), and the $\frac{\text{Height}}{\text{Width}}$ index (28) of the palates of infants under one year of age, and may serve as a basis for further studies on the pathogenesis of malocclusion, mouth breathing and attendant facial malformations.

I wish to thank Dr. Stanton for the use of his apparatus and equipment and for numerous courtesies during the course of the work.

CONGENITAL GOITER

REPORT OF FOUR CASES

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Congenital goiter was first described by von Ammon,[1] with Heinrich Adelmann as a collaborator, in 1839. From this time to the present day about one hundred cases have been reported, but there has been little or no advancement in the etiology of the condition. Following von Ammon's original work, many papers were published during the nineteenth century. Demme and Dorr, in reports from the Jener Hospital at Berne, published fifty-six cases of goiter in the new-born between 1862 and 1884; twenty-seven of these cases appeared in boys, and twenty-nine in girls. Commandeur[2] noted twelve cases, all of which appeared in perfectly developed children. About the same time Fabre and Thevenot,[3] after a careful search of literature, gathered 130 cases published up to that time. Two cases were reported by Peterson.[4] They are chiefly of surgical interest.

There are two theories as to the origin of congenital goiter: (1) by the earliest authors it was considered as being purely hereditary; but, (2) more recent investigations show that congenital and endemic goiters are closely related, and that they may be of common origin. The fact that goiterous mothers, living in nongoiterous communities, never bear children in whom a goiter is present, strongly disproves the theory that goiters are purely hereditary. It does not disprove an hereditary predisposition to the growths in later life, or while the fetus is developing in utero.

With the close relationship between congenital goiter and the endemic form in mind, it seems most plausible to investigate the evidence that is at hand relating to the very common endemic variety. Two modern views exist: (1) that endemic goiter is produced by metabolic disturbances closely related to iodin metabolism, and (2) that it is due to some form of infection.[5] In either event, it is believed that the water supply has a very close connection with the causation, either in the failure of the mineral content to meet normal metabolic requirements, or in containing the infectious organism. In goiters the thyreoglobulin has been shown to be markedly deficient in iodin content, and this deficiency is believed to be due to the low amount of iodin in the

1. Von Ammon, F. A.: Die angeborenen chirurgischen Krankheiten des Menschen, Berlin, 1839 **1**:53-59, Pl. xiii.
2. Commandeur: Bull. Soc. d'obst. de Par. **11**:103, 1908.
3. Fabre and Thevenot: Rev. de Chir. Par. **37**:781, 1908.
4. Peterson: Arch. Pediat. **28**:142, 1911; Med. Rec. **90**:789, 1916.
5. McCarrison: Proc. Roy. Soc. Med., Lond., 1908; Lancet **1**:147, 219, 365, 1913; Practitioner **94**:70, 1915.

so-called "goiter waters," although the chemical examination of water from goiterous and nongoiterous districts close by showed no difference in mineral content. And further, Fenger [6] shows that the thyroid of a normal human fetus is almost entirely devoid of iodin.

Certainly, as far as congenital goiter is concerned, those who cling to the theory of infectious origin seem to have the greater weight of evidence in their favor, though it must be acknowledged that the sum total of evidence is quite meager. The epidemic form of goiter seems closely allied to an infection of some form. Summers,[7] in this country, nicely produces many arguments in favor of the infectious theory, and recapitulates the findings of a number of investigators in the experimental field to show that this theory is the most logical one. He points out that pregnant animals drinking goitrogenous waters, though escaping themselves, have brought forth goiterous progeny; that the water is made inactive at 70 C., which is much lower than one would be led to believe that mineral decomposition would take place, and he finally concludes that the goiter is transmitted to the fetus in utero. Furthermore, the weight of such an authority as McCarrison,[5] who as early as 1908 stated that of all the infectious diseases which impair the unborn child's thyroid mechanism the most important is endemic goiter, should lead us to investigate more closely the theory of infectious origin. However, until the etiologic organism is isolated and Koch's postulates are fulfilled, we can do little more than say that this is a likely and plausible hypothesis.

REPORT OF CASES

Our patients came from the southwest section of Virginia where endemic goiter is prevalent.

Family History (For the group).—Mother dead, cause unknown; she had had a large goiter as long as her eldest daughter could remember. Father living but has heart disease; he is a chronic alcoholic. There are six children; the eldest, a girl, aged 19 years, is without goiter. She reports that she "has never had any swelling in her throat." The youngest child, a female, aged 18 months, has no goiter. The other four children are boys.

Case 1.—J. C., white male, aged 3½ years. The only disease he has ever had was measles; there is also a susceptibility to "colds." He does not complain of the enlarged thyroid, though it is said that this has been present since birth.

Physical Examination.—The patient is a well developed white boy, well nourished, and showing no sign pointing to endocrinopathy.

The head is of normal size and contour; the hair is normal in appearance and distribution. The eyes are entirely negative; Stellwag's, Joffrey's and von Graefe's signs are negative. The expression is normal, being neither cretinoid, myxedematous, nor suggestive of hyperthyroidism. The oral cavity is normal, except for a small amount of adenoid tissue in the pharyngeal vault; the tonsils were neither enlarged nor infected; the teeth were in fair condition, and the tongue was not enlarged or protruding.

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6. Fenger: J. Biol. Chem. **11**:489, 1912; **12**:55, 1912; **14**:397, 1913.
7. Summers: Ann. Surg. **62**:138, 1915.

The thyroid gland was generally enlarged, though most marked in the region of the isthmus; its consistency was soft and resilient, and there were no nodules. The posterior cervical, axillary and inguinal lymph glands were enlarged, though neither tender nor immobile. The skin was normal in appearance, and the amount of perspiration was neither increased or decreased. The nails, too, were entirely normal.

The chest was normal on inspection, and the cardiac impulse was perceptible in the fifth left interspace about 2½ inches from the midsternal line. The lungs were negative. Nothing abnormal could be noted in the heart, and the general vascular system was negative.

The abdomen was normal. The genitals were well developed but not overdeveloped.

The extremities showed nothing abnormal. The hands were well developed, and they were neither thickened nor clumsy. The legs were normally developed, and the knee-jerk was normal; the gait was normal.

Fig. 1.—Case 1.

Fig. 2.—Case 2.

There was no sign of mental weakness, imbecility, or defectiveness of the special senses.

Roentgen-ray examination for enlarged thymus showed only the normal condition. The sella turcica was normal

Laboratory Examination.—Differential count: Polymorphonuclears, 52 per cent.; small lymphocytes, 38 per cent.; large lymphocytes, 3 per cent., and eosinophils, 7 per cent. Hemoglobin, 55 per cent. Examination of feces showed ova of *Ascaris lumbricoides.* The other laboratory findings were normal.

Case 2.—E. C., white male, aged 6 years.

History and physical examination identical with findings in youngest boy, with the following exceptions: He had had whooping cough as well as measles. At the present time he has a troublesome, hacking cough, which was temporary and accompanied a cold. Thyroid was identical in consistency and shape with that in the first case.

Laboratory Examination.—Differential count: Polymorphonuclears, 60 per cent.; small lymphocytes, 35 per cent.; large lymphocytes, 2 per cent., and eosinophils, 3 per cent. Hemoglobin, 60 per cent. The feces showed ova of *Ascaris lumbricoides.*

CASE 3.—T. C., white male, aged 8 years.

Report identical with that of Case 2, except that this boy was not troubled with a hacking cough.

Laboratory Examination: Differential count: Polymorphonuclears, 84 per cent.; small lymphocytes, 10 per cent.; large lymphocytes, 3 per cent.; eosinophils, 3 per cent. Hemoglobin, 70 per cent. Feces showed ova of *Ascaris lumbricoides* and *Tricocephalus dispar.*

CASE 4.—I. C., white male, aged 14 years.

History and physical examination the same as in previous cases, except that thyroid is only moderately enlarged. The enlargement here is general, as in the other cases, and the isthmus likewise is the most prominent part of the gland; consistency similar to that of the gland in previous cases.

Laboratory Examination.—Differential count: Polymorphonuclears, 61 per cent.; small lymphocytes, 28 per cent.; large lymphocytes, 2 per cent., and eosinophils, 9 per cent. Hemoglobin, 60 per cent. Feces showed ova of *Ascaris lumbricoides.*

Fig. 3.—Case 3.

Fig. 4.—Case 4.

The absence of toxic thyroid symptoms or other endocrinopathy is especially to be noted in these cases, and the lack of pressure symptoms is quite remarkable. The fact, too, that goiter appeared only in the male children is very striking, if it is only a coincidence; the literature shows no relation whatever of goiter to sex, except that it is, perhaps, more frequent in females. The finding of *Ascaris lumbricoides* in all four cases is also noteworthy. Although there was a slight general enlargement of all the lymph glands in Case 1, this does not seem to be of great significance, since neither symptoms nor signs of any complicating disease existed, and the roentgenograms of this, as well as the other three cases, showed a normal condition of the thymus and the sella turcica. All the goiters were symmetrically enlarged, the most prominent part being the isthmus; their consistency was soft, and they were suggestive of goiters of the colloid type.

THE ETIOLOGY AND TREATMENT OF AMMONIA DERMATITIS OF THE GLUTEAL REGION OF INFANTS *

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All those who treat infants and young children encounter with more or less frequency instances in which the diapers after having been wet with urine for several hours give off the odor of ammonia. Frequently the odor is faint and the condition occurs in infants otherwise well and thriving. In some cases the ammoniacal odor is very pronounced and accompanied by irritation of the skin of the diaper region usually more marked over the buttocks and inner surfaces of the thighs. The lesion may consist only of diffuse redness but not infrequently vesicles and papules with more or less excoriation occur. There seems no doubt that the dermatitis is caused directly by the ammonia. Attention was called to the condition by Southworth [1] and it has been discussed in some detail by Zahorsky [2] and more recently by Brennemann.[3] The latter observer has described especally the ulceration at the external urinary meatus that may occur in circumcised male children in association with the ammoniacal diaper, a lesion noted previously by Zahorsky.

The characteristic lesions of the diaper region have long been recognized and have been described under a variety of names, but have not generally been attributed to ammonia in the napkin. It was formerly frequently confused with the lesions of hereditary syphilis and Parrot, who was one of the first to describe the condition, mistook it for a lenticular syphilide. Jacquet,[4] however, clearly differentiated these eruptions of the diaper region from syphilitic lesions. He divided them into simple erythematous, erythemato-vesicular or erosive, papular or post-erosive and ulcerative forms all of which are stages of one process and may overlap or coexist in the same patient. Finkelstein [5]

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1. Southworth, T. S.: The Ammoniacal Diaper and Its Correction, Arch. Pediat. **30**:730 (Oct.) 1913.

2. Zahorsky, J.: The Ammoniacal Diaper in Infants and Young Children, Am. J. Dis. Child. **10**:436 (Dec.) 1915.

3. Brennemann, J.: The Ulcerated Meatus in the Circumcised Child, Am. J. Dis. Child. **21**:38 (Jan.) 1921.

4. Jacquet, L.: Traité des Maladies de l'Enfance. Paris, 1905, 4, 714. Graucher et Comby.

5. Finkelstein, H.: Lehrbuch der Säuglingskrankheiten. Part 2, p. 588. Berlin, 1912.

prefers the term "dermatitis papulovesiculosa glutealis infantus" to other previous names such as "erythème papuleux" (Parrot), "erythème lenticulaire" (Sevestre) and "erythème papulex fessier post-érosif" (Jacquet). In all these, the lesions are apparently identical with those due to ammonia irritation, and although no reference is made to an ammoniacal diaper as being associated with the condition, there seems little doubt from the descriptions given that examination of the wet diapers in such infants would have been followed by a recognition of the ammonia odor. One possible explanation for such lack of detection of the characteristic odor is suggested by the assumption that most of the recorded observations were made on infants after admission to hospitals. Under proper conditions of cleanliness and hygiene in a hospital ward the ammoniacal odor disappears and the lesions heal rapidly for reasons that will be apparent later.

The lesions as described by Finkelstein are limited to the diaper region and consist of rounded or oval raised papules of a red or bluish-red color. The surface of the papule may be smooth but is frequently eroded. Around or near the papules, vesicles are frequently found, and it is probable that the vesicles, papules and ulcers are different stages of the same lesion. After a shorter or longer interval the lesions regress and leave brownish pigmented spots. He calls attention to the fact that E. Fournier [6] reproduces a picture of a typical case of such papulovesicular dermatitis as an illustration of an ulcerating syphilide.

A more complete description of the various forms of the lesions is given by Adamson [7] who mentions also the severe ulcerative erosions that occur in the occasional advanced or neglected cases with deep punched-out and sharply marginated ulcers that may be circular or oval or more often coalesce to form vermicular or polycyclical lesions. He also calls attention to the constant distribution of all the lesions on the convex surfaces of the napkin region and the contrasting freedom of the flexures and sulci between them as strongly suggesting some irritating factor associated with the wet napkin. This assumption is strengthened by the fact that not infrequently in these infants erythematous patches may develop on the calves and heels from contact with the external surface of the napkin. In addition, this author reviews the features that distinguish these eruptions from those of hereditary syphilis. These are: (1) the striking limitation of the eruption to the convex surfaces of the diaper region and the absence of lesions on the face, palms and soles and at the anal margin; (2) the

6. Fournier, E.: Recherche et Diagnostic de l'Hérédo-Syphilis Tardive. p. 157. Paris, 1907. Masson and Cie.

7. Adamson, H. G.: On Eruptions of the Napkin Region in Infants, with Especial Reference to the Diagnosis of the Eruptions of Congenital Syphilis from Certain Nonspecific Napkin-area Eruptions of Common Occurrence, Brit. J. Dis. Child. **5**:13 (Jan.) 1908.

absence of the coppery color of syphilitic eruptions and the absence of snuffles, rhagades, skin opacity, glandular enlargement, and other signs of syphilis, and (3) the variation in the course of the erythematous lesions which frequently tend to disappear without antisyphilitic treatment. It might be added that these lesions rarely occur in nursing infants and are far more commonly found during the latter part of the first year or later while syphilitic eruptions occur, as a rule, much earlier. The Wassermann reaction, also, renders the differentiation of the two conditions relatively simple.

The production of these lesions has been attributed by Leopold [8] to local irritation from soap alkali remaining in diapers from an insufficient rinsing, and he states that a rapid cure follows the elimination of this factor. Finkelstein, on the other hand, reports that his attempts to substantiate such an hypothesis have been fruitless. All agree that the etiologic agent is connected in some manner with the diaper, and many believe that there is also an association with some nutritional disorder.

Although the ammoniacal napkin or its accompanying dermatitis is familiar to many, the etiology of the condition is obscure, and the treatment, consequently, is not always effective. In general, the explanation usually given attributes the condition to a nutritional disorder with acidosis and increased ammonia excretion in the urine. The liberation of this ammonia by alkali in the diaper is assumed to result either from soap left after washing or from alkaline stools. This theory is apparently supported by the fact that many infants with ammoniacal diapers present the clinical picture of overfeeding with fat or with milk, which has been described by Czerny and Keller as "milchnährschaden." Here alkaline stools and an increased excretion of ammonium salts occur, and it is true that by placing such infants on a diet containing relatively less fat or protein the odor of ammonia frequently disappears from the napkins. On the other hand, ammoniacal diapers occur with some frequency in infants otherwise thriving, and dietetic measures, alkali therapy and careful exclusion of alkali from the diapers fail to correct the condition in a great many cases.

It has been assumed by many that bacteria such as the *Micrococcus ureae* are in some manner concerned in the production of ammonia in the diaper by breaking up urea, and Brennemann has suggested that the thorough boiling of diapers daily might lessen ammonia production. No microorganisms, however, have been isolated in connection with these cases.

In this paper the results of a bacteriologic study on infants with ammoniacal diapers are given. A urea splitting organism has been

8. Leopold, J. S.: Dermatitis Excoriativa Infantum. A Common Eruption of the Napkin Region in Infants, Arb. z. 10 jähr. Bestehen d. Kinderasyls d. Stadt Berl., p. 105, 1911.

isolated from the stools of a number of such infants, and it has been demonstrated that the formation of ammonia in the diapers can be prevented in all such cases by a relatively simple procedure.

Methods.—The cases studied included infants and children from the St. Louis Children's Hospital and the Washington University Dispensary with a number of cases obtained through the courtesy of members of the hospital staff. Specimens for culture were secured in most instances by inserting a sterile glass tube into the rectum and obtaining some small particles of fecal matter. In other cases cultures were made from urine brought in by physicians or by patients.

The culture medium used was fresh urine to which phenolsulphonephthalein was added as an indicator. It was sterilized by filtration through a diatomaceous filter and had an acid reaction. Tubes of this medium were inoculated with a small portion of feces or with urine and incubated at 37° C. After twenty-four hours, if the reaction had become alkaline, several loopfuls were inoculated into a fresh tube of medium and reincubated. When the production of alkali had persisted through several tubes, some of the material was seeded on plain agar plates and a number of colonies picked and inoculated into urea medium. This latter was composed of urea, 1 per cent. and 0.2 per cent. each of calcium chlorid, monosodium phosphate, dipotassium phosphate and magnesium sulphate with phenolsulphonephthalein added as an indicator, and sterilized by filtration. The production of an alkaline reaction by growth in this medium was always due to ammonia production.

Sterilization by filtration was rendered necessary by the fact that urine is decomposed by heat sterilization with liberation of ammonia and precipitation of phosphates. The technic of isolation is relatively simple. Addition of urea and indicator to the agar for plating in order that the urea fermenting organisms might be quickly differentiated by the color change produced from the alkali, is not practicable since the ammonia produced is volatile and quickly diffuses through the whole plate. The organisms grow much more readily in urine than in the urea salt medium and the former is to be preferred for the original multiplication before isolation.

Results of Cultures.—The results of the cultures from stools of infants with ammoniacal diapers and of older children with enuresis and ammoniacal decomposition of the urine are given in Table 1. In all, thirty-one infants and children with this condition were examined. Some had merely an ammoniacal odor to the morning diapers, some showed in addition an erythema while in others typical vesication or excoriation and ulceration were noted. Four of the latter group were male infants with an ulceration and crust of the external urinary meatus in addition to other lesions. Of the thirty-one cases, 18 were boys and 13 girls; 5 had the odor to diapers only; 15 had a mild dermatitis, and

11 had a more severe lesion with blistering; 5 were under 6 months of age, 7 were from 6 to 12 months old, 14 were in the second year and 5 were over 2 years, the oldest being 4. Only one infant of this series was exclusively breast fed. Although the series is not large, the results of cultures were so uniform and constant that further multiplication of cases seems unnecessary. Urea splitting bacteria were isolated in pure culture from the feces in all cases examined, and almost without exception the organism involved in every case is the same, or a closely related strain. It will be noted that in about half the instances the organism was not isolated on the first examination but was obtained from a later specimen. These failures were in the cases first studied.

TABLE 1.—AGE AND SEX OF INFANTS AND CHILDREN WITH AMMONIACAL NAPKINS AND DERMATITIS FROM WHOM *B. ammoniagenes* WAS ISOLATED

No.	Age	Sex	No. of Specimens Examined	Dermatitis	Remarks
1	1½ mos.	M	1	Severe	
2	1½ mos.	F	1	Severe	Exclusively breast fed
3	2 mos.	F	3	Moderate	
4	2½ mos.	M	1	Severe	Partly breast fed
5	4 mos.	M	1	Severe	
6	6 mos.	M	1	Moderate	Partly breast fed
7	9 mos.	M	1	Severe	
8	9 mos.	F	1	Severe	
9	9 mos.	M	3	None	
10	10 mos.	M	2	Severe with meatus crust	
11	10 mos.	M	1	Moderate	Bacillus in urine also
12	12 mos.	M	2	Moderate	Twin
13	12 mos.	M	2	Moderate	Twin
14	12 mos.	F	3	Severe	
15	12 mos.	F	1	Moderate	
16	12 mos.	F	1	Moderate	
17	15 mos.	M	1	Severe with meatus crust.	Urine showed bacillus and S. lutea
18	16 mos.	F	2	Moderate	
19	18 mos.	M	2	None	
20	18 mos.	F	1	None	
21	18 mos.	M	1	None	Enuresis
22	19 mos.	F	3	None	
23	19 mos.	F	1	Severe	
24	20 mos.	M	1	Severe with meatus crust	
25	21 mos.	M	3	Moderate	
26	22 mos.	M	1	Severe with meatus crust	
27	2 yrs.	F	3	Severe	
28	2½ yrs.	F	2	Moderate	
29	2½ yrs.	F	1	Moderate	Bacillus from urine also
30	2¾ yrs.	M	2	Mild	
31	4 yrs.	M	2	Severe	

As more experience in the isolation was acquired, the organism could be found practically always on the first trial

The organism constantly present is an aerobic, nonmotile, gram-positive bacillus which does not ferment the ordinary sugars, nor form spores. Most of the strains isolated show a faint yellowish pigmentation in culture. Morphologically, the organism is a rather short straight rod with well rounded ends, the majority of the elements measuring 0.8 x 1.4 microns. Occasional longer forms are encountered and in older cultures involution shapes are common. These may be as long as 4 microns, sometimes are pear-shaped or otherwise irregular and occasionally unevenly stained. Cultures grow well at

both room and incubator temperatures. When grown on urea-containing media, the alkalinity reaches a p_H of 9.3 at which point growth is considerably inhibited. Even moderate degrees of acidity cause a definite inhibition of growth. The name *Bacillus ammoniagenes* is suggested for the organism.

Other organisms exerting a similar action on urea are the *Staphylococcus aureus* and *S. albus* (the latter being identical with the *Albococcus ureae*) *B. smegmatis, Sarcina lutea* and *B. proteus.* The *Sarcina lutea* was isolated once from a urine specimen from one of these children but *B. ammoniagenes* was also present. *B. proteus* has not been found in any of the cases with ammoniacal napkins, nor have the other organisms mentioned been found in the stools examined.

A number of controls have been examined in order to determine the general incidence of the organism. In twenty-five exclusively breast fed infants under 6 months of age, the bacillus was found only once. A similar number of bottle fed infants under two years of age in whom there was no complaint of ammoniacal urine, showed the presence of the organism in the stools in about one-fourth of the cases, while in thirty-four older children it was found in one half the cases. Apparently, its distribution is extensive and any infant may harbor it. Under conditions that are favorable for the organism, as, for example, a lack of acidity of the intestinal contents, the number increases greatly and the diaper region may become infected from the stools.

The inhibiting effect of acid on the growth of this organism is striking and is shown in the Table 2 in which the growth is compared with that of *B. coli.* Broth of varying p_H was inoculated so that one c.c. contained between 500 and 1,000 organisms and counts made at the end of twenty-four hours at 37 C. (Table 2). It will be noted that although acidity inhibits the growth of *B. ammoniagenes* very considerably, the organism grows very abundantly in alkaline mediums between the ranges of p_H 7.0 and 8.5. The effect of the reaction of the medium on the growth of *B. ammoniagenes* has been shown in several experiments, of which that given in Table 2 is typical.

The constant presence of a saprophytic urea splitting bacillus in the stools of infants with ammoniacal diapers suggests the obvious explanation for the condition. The frequent soiling of the gluteal region with feces gives an opportunity for this organism as well as the other intestinal bacteria to contaminate the skin of this area. The extent of this seeding must depend in part on the degree of infestation of the intestine with the bacillus and probably also on the care used in keeping the infants clean. With the wetting of the napkin by urine, an excellent culture medium is furnished at a favorable temperature and the contaminating bacteria multiply with corresponding rapidity. The products formed during the growth of most of the intestinal organisms

have no irritant action but when urea-splitting bacteria are present, there is a production of ammonia [9] with consequent irritation of the skin. Such growth in the urine must contaminate the adjacent skin still more extensively and subsequent formation of ammonia in a similar manner serves to accentuate both the odor to the napkins and also the dermatitis.

Clinical observations corroborate this hypothesis. For example, the well-known association of ammonia formation with the wet diaper in situ only, and the common observation that it is especially in the morning that the ammoniacal odor is most striking and that the erythema is first noticed. It has been mentioned that *B. ammoniagenes* grows actively at a temperature of about 30° C., and consequently the longer incubation in the night diaper allows correspondingly more ammonia formation.

TABLE 2.—EFFECT OF THE REACTION OF CULTURE MEDIUM ON THE GROWTH OF B. AMMONIAGENES

P_H	B. ammoniagenes	B. coli
6.0	2,300	190,000
6.5	90,000,000	300,000,000
7.0	330,000,000	410,000,000
7.5	290,000,000	181,000,000
8.0	271,000,000	54,000,000
8.5	275,000,000	35,000,000
9.0	64,000,000	500,000
9 5	7,500,000	1,000

It might be expected that the ammonia formation even in infested infants would be influenced by a number of factors. For example, the care observed in keeping the infant clean, the length of time elapsing before the wet napkin is changed after soiling, whether the napkins are boiled or merely rinsed out, as well as other conditions may serve to explain the occasional vagaries observed in the appearance of the ammoniacal odor on some occasions and its disappearance at others. To some of these factors also may be attributed the rapid amelioration of the condition when the infant is placed under the strict hygienic regimen of a hospital.

Another factor that is of considerable importance is the diet. Mention has been made of the observation that many infants with ammoniacal diapers are fed on formulas relatively high in fat or milk and that the condition does not occur in breast fed infants. It seems quite probable that the reaction of the intestinal contents, especially that of the large intestine, influences the number of urea-splitting bacilli found in the stools. The only experimental evidence of this is somewhat indirect and consists of the observation that the growth of

9. Ammonia is derived from urea as a result of the following well-known reaction: $CO(NH_2)_2 + 2H_2O = (NH_4)_2CO_3 = 2NH_3 + H_2O + CO_2$.

this organism is inhibited in acid medium but abundant in neutral or alkaline medium. Apparently, then, any factors in the diet which would tend to make the stools alkaline would favor the multiplication of the organisms while acid intestinal contents would inhibit their growth. Such an hypothesis would explain the improvement of the condition when relatively less fat or milk is fed or relatively more sugar, and the rarity of the complaint in breast fed infants in whom the stools are usually acid. Obviously, however, the diet is only one of the factors by which the presence of these organisms is influenced and, although its regulation is frequently followed by a marked improvement, this alone does not always completely eliminate the production of ammonia.

It seems unnecessary to assume a high ammonia content of the urine since the mechanism for formation of ammonia from urea is apparently constantly present. Ammoniacal fermentation of the urine occurs not only in the diapers of healthy infants but in the clothing and bedding of older children with enuresis. Only a few of the latter were observed in this series and urea-splitting bacilli were isolated from the stools in each instance. The production of ammonia by bacterial action on the urea cannot, of course, liberate the combined ammonia normally present in the urine. In order for ammonia derived from the ammonium salts of the urine to be freed, the presence of some other alkali is necessary either in the stool or in the diaper. The possibility of small amounts of ammonia being liberated in this manner in certain instances cannot be denied, and in such cases the alkaline reaction would greatly favor the growth of the urea splitting bacillus.

Although there seems no doubt that the skin lesions are caused by the ammonia and not by the bacteria, this has been definitely established experimentally. The method used is briefly as follows: Gauze saturated with (1) a broth culture of the organism (*B. ammoniagenes*), and (2) 1 per cent. urea in broth, freshly contaminated with a pure culture of the same bacillus, were used in separate experiments. The gauze was applied to an area about 10 cm. square on the inner surface of the forearm of an adult, covered with rubber tissue and a bandage, and allowed to remain over night (sixteen hours) on two successive days.

The broth culture of *B. ammoniagenes* caused no skin irritation, while that to which urea was added caused a slight but definite erythema after the first application and a marked diffuse scarlatiniform erythematous dermatitis after the second. With the development of the dermatitis there was moderate burning and itching, and the dressings when removed were quite ammoniacal. As the dermatitis regressed, the skin showed the characteristic glistening, slightly wrinkled appearance which is frequently seen in the healing eryth-

ematous lesions of the gluteal region in infants. No attempt was made to reproduce the lesions experimentally on infants. It seems probable that the development of the more severe ulcerative lesions requires repeated irritation over a period of several days.

Treatment.—Since the dermatitis in these cases is a result of ammonia formed by bacterial action on urea in the diaper, it follows that the simplest and most logical method of prevention is to treat the diaper and not the infant. In the experiments for determining the easiest and most effective means for such treatment the following general method was employed. Ordinary diapers twenty-four inches in diameter were soaked in the inhibiting agent, wrung thoroughly and allowed to dry. Depending on the thickness of the material, diapers of this size retain from 75 to 150 c.c. fluid. In the tests the dry napkins were moistened with fresh urine to which sufficient bacteria (*B. ammoniagenes*) from an agar culture had been added to give a slight turbidity. Each was placed in a separate, loosely covered receptacle and incubated over night at 37 C. The organism used in all instances was the urea splitting bacillus isolated from stools of children with ammonia dermatitis. Controls of untreated napkins with inoculated and with uninoculated urine were included in every series. After incubation, ammonia when present was usually easily recognizable by the odor although slight amounts were always confirmed with moistened litmus paper. When no alteration of the litmus paper placed in the receptacle was observed after several minutes, it was considered that no ammonia had been found. Usually the presence of ammonia was easily recognized.

The formation of ammonia from urea by bacteria must be accomplished by the action of urease furnished by the organisms and the earlier experiments were directed at inhibiting the action of this ferment. Two metallic salts which exert the most striking inhibitive effect on urease activity are mercuric chloride and copper sulphate and these were tried in varying strengths with urease solutions and with living bacterial suspensions in incubated diapers. It seems unnecessary to give the experiments in detail. Copper sulphate gave practically complete inhibition of urease activity in dilutions of 1 : 1,000 but in higher dilutions the inhibiting action was only partial. In the diaper with urine and bacteria, unless the strength of the solution was more than 1 : 1,000, the ammonia odor was pronounced. With mercuric chlorid practically complete inhibition of ammonia formation occurred in the diapers with dilutions as high as 1 : 30,000 although sometimes faint traces were detectable by litmus paper.

Later, when an attempt was made to extract the urease from massive growths of the organism, it was found that this ferment resembles other bacterial enzymes in being intracellular and that it does not

diffuse out into the surrounding medium. It can be demonstrated in dried dead organisms but its action normally is apparently dependent upon metabolism during cell growth and is probably intimately connected with vital bacterial activity. The inhibition of ammonia formed by bacterial action in the diaper, therefore, depends rather on the inhibition of bacterial growth than upon inhibition of urease activity. Consequently, the superiority of mercuric chlorid over copper sulphate in the previous experiments is apparent.

This was further shown by the action of boracic acid which in dilutions of 1 : 300 practically completely prevents ammonia formation in the diaper through inhibition of bacterial growth. Other antiseptics, such as argyrol, also inhibit ammonia formation in a similar manner in dilutions of 1 : 800 while the same is probably true of other bactericidal substances. Phenol is volatile and the amount left in the diaper after drying is not sufficient to inhibit ammonia formation even when used in a concentration of 1 per cent. A most efficient action is obtained with mercuric iodid which, however, appears to have no greater inhibiting effect than the mercuric chlorid.

In the treatment of infants with dermatitis due to ammonia found in the diaper, two of the substances found effective in the above experiments have been used to prevent further ammonia production. These were mercuric chlorid and boracic acid. After washing, the diapers were soaked in the solution, wrung thoroughly and dried. In the milder cases only the napkins used at night were so treated, while for the more severe cases all napkins were impregnated with the antiseptic. In the majority of instances mercuric chlorid has been used and the results have been excellent. In dilutions of 1 : 10,000, however, there was not always complete suppression of ammonia formation, but the use of 1 : 5,000 dilutions was uniformly followed by the disappearance of the ammonia odor. Occasionally, the mothers reported that by careful examination they could detect faint traces of the gas in the morning diaper after starting the treatment, but otherwise, as nearly as one could determine from questions, the ammonia formation stopped abruptly with the use of the antiseptic. The necessity for using the solutions in the diaper on the infant stronger than those which prevented growth of the organisms experimentally is not clear. One possibility is that since the infant's urine passes into the napkin at the area nearest the urethra, much of the antiseptic dissolved by the first flow of urine may be carried out into other portions of the cloth. The small amount of mercuric chlorid left in the urine later excreted into the central portion may be insufficient to inhibit bacterial growth. Such an explanation, however, is purely speculative.

The treatment by mercuric chlorid impregnation of the diaper has been carried out in a number of instances in the pediatric clinic of the Washington University Medical School and also by members of the

pediatric staff in their practice. In all more than fifty infants with ammoniacal diapers, many of whom had also an erythematous or papulovesicular dermatitis, have been treated, and the disappearance of the ammonia and of the dermatitis has followed quickly in all instances. Two characteristic examples will serve to illustrate the effect of this treatment:

CASE 1.—A 5 months old infant artificially fed at four hour intervals on a whole milk formula and thriving, awakened three or four times nightly, and on each occasion cried until the mother replaced the wet napkin with a dry one. The wet diapers had a strong ammoniacal odor and the infant's buttocks and thighs showed an erythematous rash with an occasional raised papule having a slightly eroded surface. When seen a week later, the eruption had disappeared and the mother reported that with the use of mercuric chlorid in the diaper, the ammoniacal odor had ceased to be noticeable and that the baby slept uninterruptedly through the night.

CASE 2.—A slightly undernourished baby, 7 months old, receiving somewhat more than a quart of whole milk daily, was brought to the clinic with the complaints of failure to gain, irritability, and constipation. The diapers were strongly ammoniacal and the gluteal region showed a characteristic papulovesicular eruption with moderate excoriation. The diet was left unchanged temporarily, and mercuric chlorid 1-5,000 prescribed in the diapers. A week later, the dermatitis was very much improved and the ammonia no longer could be detected. The other symptoms, however, were still present and were relieved by a suitable milk formula.

In some instances the ammoniacal odor to the napkins reappeared when the use of the antiseptic was discontinued but in others no further evidence of ammonia was noticed. Even in the more severe cases treatment of the night diapers only was sufficient after a few days. No evidence of any skin irritation attributable to the mercuric chlorid was ever observed. No older children with enuresis and ammoniacal fermentation of the urine have been treated in this series, although in such cases the use of some modified form of diaper impregnated with the antiseptic would appear advisable, especially if skin irritation is present.

Boracic acid was tried on only a few infants so that its action has not been observed in sufficient cases to allow a proper estimate of its value. In the instances in which it was employed, however, a very marked inhibition of ammonia formation was noted with dilutions of 1:20. Argyrol was considered somewhat unsuitable on account of the discoloration of the napkins. Mercuric iodid has not been employed from lack of sufficient cases, although the experimental evidence indicates that dilutions of 1:5,000 should prove very efficient. The administration of hexamethylenetetramine has not been attempted in this condition on account of the relatively large doses required to render the urine constantly antiseptic. Its use does not seem advisable for such a purpose since the employment of antiseptics in the diaper is followed by such good results.

In the practical use of the antiseptics it should be remembered that the diapers will retain from three to five ounces of fluid after thorough

wringing and a corresponding dilution of the antiseptic solution occurs when wet diapers are placed in it. The following directions have been given regarding the use of the three antiseptics:

Mercuric chlorid (1:5,000).—Dissolve one 7½ grains tablet in two quarts of water and use this solution for the final rinsing of the diapers. Wring thoroughly and dry.

Boracic acid (1:20).—Dissolve one heaping teaspoonful in six ounces of water by warming. Pour this over a dry napkin, wring thoroughly, and allow to dry.

Mercuric iodid (1:5,000).—An aqueous solution of 5 per cent. each of mercuric iodid and potassium iodid is prescribed. One teaspoonful is to be added to a quart of water and used for the final rinsing of the diapers.

The correctness of the assumption of an atiological relationship between urea splitting bacteria and the presence of ammonia in the diaper with consequent skin irritation has been further confirmed, therefore, by the inhibition of ammonia formation in the presence of antiseptics in the diaper.

SUMMARY AND CONCLUSION

The common erythematous or papulo-vesicular dermatitis of the gluteal region in infants is caused by ammonia in the diaper and should be classed with other forms of dermatitis venenata. A similar dermatitis may occur in older children who have enuresis, and this, also, is associated with the presence of ammonia in the clothing or bedding wet with urine.

In both infants and older children with this affection, a characteristic gram-positive bacillus has been isolated from the stools in every case examined. This organism is a saprophyte but has the property of fermenting urea with the production of ammonia. It has been called *B. ammoniagenes.*

In a series of infants without ammonia formation in the diapers this organism can be found relatively infrequently; in older children, however, its occurrence is not unusual.

The use of diapers impregnated with an antiseptic such as mercuric chlorid, causes a prompt disappearance of the ammoniacal odor and a rapid regression of the skin lesions.

The evidence presented indicates that "the ammoniacal diaper" and the dermatitis that accompanies ammoniacal urines are dependent on bacterial fermentation of urea. The microorganism concerned is apparently the same in all cases and infests the diaper from the feces. This infestation can readily be suppressed and the ammoniacal fermentation eliminated by the use of antiseptics in the diaper. With the cause thus removed the dermatitis rapidly disappears.

THE ABDOMINAL PAIN OF THROAT INFECTIONS*

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The purpose of this paper is to direct attention to a symptom that in my experience and in that of my immediate associates is of very frequent occurrence and which has, so far as I know, received little, if any, attention in the literature. Several recent exhaustive papers on the subject of abdominal pain in children do not mention it and a partial search of the literature would lead one to think that others have either not made the same observation or else have failed to consider it as a distinct entity worthy of record. For nearly ten years this symptom has so regularly and so insistently intruded on our attention that it has seemed to me worth while to discuss it on an occasion like this.

The symptom to which I refer is that of abdominal pain occurring often to the exclusion of all other subjective symptoms, or, at least, complaints, in the course of throat infections in children. By throat infections I mean that whole series of upper respiratory tract infections that grades imperceptibly from the common cold to a fatal septicemia beginning in the throat, and that constitutes easily the bulk of the practice of the general practitioner and of the pediatrician, who makes house calls. In the course of these infections, as we know so well, we may have a formidable array of manifestations depending on the localization or extension of the original infection. Among these are coryza, pharyngitis, tonsillitis, postnasal infection, laryngitis, bronchitis, sinus infections, otitis media, mastoiditis, sinus thrombosis, meningitis and encephalitis by extension, retropharyngeal and peritonsillar abscess, cervical adenitis, stomatitis, conjunctivitis, pneumonia and pleurisy; and more distantly carditis, arthritis, myalgia, enteritis, peritonitis, appendicitis, mesenteric and retroperitoneal lymphadenitis, nephritis, pyelitis, pyemic abscess, hematogenous encephalitis and meningitis, erythemas, purpuras, and finally, a septicemia of unascertainable localization that may last for months, or prove rapidly fatal under the clinical picture of a generalized streptococcemia.

Among the sporadic cases of this nature many patients will complain of an abdominal pain at the beginning, during, or after the acute manifestations in the throat. Often they complain of nothing else, for it is a well known fact that children only exceptionally complain of the throat itself. This symptom attracts greatest attention to itself,

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however, in certain of those epidemic peaks of throat infections, or grippes, that we have with us several times each year when the number of these cases exceeds many fold that of all other contagious diseases put together. It is a common observation that in these flurries the genus epidemicus varies strangely. At one time nose bleeds will be very common; at another vomiting will constitute so persistent and wide spread a feature that one hears much of epidemic "acidosis"; again, peculiarly virulent otitis media will dominate the picture while it is almost absent in other epidemics; the same is true of cervical adenitis and we hear then once more of "glandular fever" as if it were a distinct entity; in other epidemics an infectious diarrhea is common; and even sepsis, nephritis, pyelitis, retropharyngeal abscess and scarlatiniform rashes show a definitely greater incidence in some epidemics than in others. The same is true of the symptom under consideration. While in nearly all of these epidemics one will find quite a few children who complain of abdominal pain, in certain epidemics this symptom rises to such importance that it occurs in nearly 25 per cent. of all the cases. At such times it is not uncommon to find several members of the family, including adults, suffering from the same thing.

The nature and location of this pain are fairly constant; the degree and time of occurrence vary much in different individuals. Sometimes it is perfectly evidently only a part of a serious infection; again it so obtrudes itself that it alone is the occasion for calling the doctor. It may occur early or late. Often it persists throughout the illness. Sometimes it apparently lasts for weaks and even months after all other symptoms have disappeared. It may be more or less constant; more often it is distinctly intermittent. It may be very slight, or the child may cry with pain over a period of hours. In the intermittent type the patient may merely screw up his face, or wince, or squirm, or turn over on his side and double up, or he may, as I have seen it a few times, scream with pain with each new attack. The abdomen is only exceptionally distended and tenderness is often absent and nearly always less marked than unelicited pain. To both of these statements there are however exceptions.

When asked where the pain is the child will quite regularly say: "In my stomach." When asked to point to it he will equally regularly place his open palm over the umbilicus. When asked to point with one finger he will again indicate the umbilicus. Exceptionally the pain is diffuse, or more on one side than on the other, or more above or below the umbilicus.

As to the cause of this pain, one can only conjecture as yet. It is not evident to ordinary clinical observation. Necropsies hardly occur where this symptom is prominent, for in the fatal cases more serious symptoms quite obscure it. Necropsies on cases dying of influ-

enza in the recent epidemics have however revealed certain interesting and suggestive conditions that can serve by analogy. In a few cases laparotomies, either frankly exploratory in nature, or equally frankly, based on a wrong diagnosis, have seemed to throw some light.

In children under 3 or 4 years of age by whom nausea is hardly distinguishable from a true pain, I believe an early abdominal complaint is often due to nausea. In the characteristic pain under consideration nausea plays no real part, as is evident from careful observation, especially on older individuals. In the early pains that are sharp and intermittent, that accompany the first objective symptoms, or even precede them, colic may be a factor. There is, however, as a rule, no evidence of indigestion, or flatulency, and such pains are not an accompaniment of other infections of like grade unless there is some evident cause as a pleurisy, or a pneumonia. I am convinced that in the causation of these abdominal pains of throat infections, indigestion, myalgia, grippy aching, neuritis, a Head zone, or a referred pain from the thorax, or from the vertebral column carried along the intercostal nerves, play no part.

In the pain that occurs most characteristically during such an infection, that lasts for some time, that even outlasts the oher evidences of the original infection, I think one must direct one's attention to the mesenteric and retroperitoneal glands. This view was first forcibly impressed on me about eight years ago. A child, aged 3½ years, had an evident upper respiratory tract infection with sore throat, otitis media, cough and bronchitis, with a low persistent temperature and no evidence of pneumonia. The abdomen was much distended, tense, painful, and tender, with no ascertainable localization. There was some vomiting. After consultation with a surgeon and other pediatricians abdominal diagnosis was deferred and operation was not considered indicated. The abdominal condition, however, became steadily worse and wholly dominated the picture. The parents became restless and an exploration in the median line seemed justified. Nothing was found except a few hemorrhagic spots on the intestines and an enlargement of the mesenteric and retroperitoneal glands. The child recovered in spite of the operation.

Shortly after this a child, aged 3 or 4 years, was seen with a slight sore throat, and a moderate otitis media. Nothing was complained of except a slight pain in the region of McBurney's point and appendicitis was suspected. There was a slight temperature, only very slight tenderness, and no involuntary rigidity. There was definitely palpable at this point a small, hard, sharply defined, freely movable mass the size of a small almond kernel, that was not very tender. It was considered an inflamed mesenteric gland, and a few days later with subsidence of all symptoms the child was allowed to go home. Within a week an

older sister presented almost identically the same picture. The same surgeon with whom I had seen the first child saw the sister about one hundred miles from town. Not daring to take the same risk, at such a distance, that we had taken with the first child who was under close observation, he operated. The appendix was easily absolved of all blame, but in the whole area explored there were a dozen or more inflamed mesenteric glands, some nearly as large as a small almond. Recovery was uneventful.

In the discussion of a recent paper of mine on abdominal pain in children, Dr. Withers of Chicago presented an interesting history. A child, aged 6 years, complained of a sore throat, and a diagnosis of tonsillitis was made by the attending physician. There was a little abdominal pain and the possibility of appendicitis was considered. Five or six days after onset, when the throat condition had receded, the child had sudden severe paroxysmal pain over the lower part of the abdomen, especially on the right side and in the region of the umbilicus. There was some tenderness and slight diffuse rigidity. The patient was then seen by Dr. Withers, who did not think the pain due to an appendix, but called in a surgeon. A diagnosis of appendicitis was made by the latter and the child was operated on. The appendix was normal. Several inflamed mesenteric glands were seen in the field of operation, one as large as a large bean, and the surgeon made an amended positive diagnosis of tabes mesenterica. The V. Pirquet test proved negative. The child was kept under observation for several years with no further evidence of any abdominal pathology.

One other case stands out especially in my memory though the evidence is inconclusive. A baby, aged 8 months, suddenly developed a temperature of 106 F. This continued between 102 and 106 F. for a period of six weeks with no other findings at any time than an initial throat infection with a slight redness of one ear drum. Drs. Abt, Walls and Shambaugh saw the case with me repeatedly. An exploration of the lateral sinus on one side was undertaken reluctantly, with negative results. At the time of this operation I palpated the abdomen carefully under anesthesia and was surprised to find between McBurney's point and the middle of Poupart's ligament a firm, freely movable, oblong mass the size and shape of a medium-sized pecan. The abdomen had been examined daily and had never been under suspicion. It did not seem possible that this mass could be an appendix and nothing further was done. Within thirty-six or forty-eight hours the whole picture changed. The child was violently ill, was prostrated, vomited, grunted with each breath, the abdomen was distended and tender and there was a large mass filling the lower part of the right lower abdominal quadrant. At the operation a few hours later a large amount of free pus was found. Conditions were such that it was not deemed wise to

explore the appendix. Unfortunately, a necropsy was not obtained. The size and free mobility of this mass, without apparent pain, tenderness and rigidity prior to the final catastrophe, together with the whole clinical setting, have always made me feel that we had to deal with a ruptured mesenteric gland, not with an appendix. Whether this child of 8 months had an abdominal pain during the illness is, of course, unknown.

That inflamed and enlarged mesenteric and retroperitoneal glands, nontuberculous in origin, do occur is well known. In his recent paper on abdominal pain in children Hutchison emphasizes the importance of enlarged glands in the causation of abdominal pain in children, but he does not relate them to throat infections That they do occur in infections having their primary seat in the throat was evident in autopsies on cases dying from influenza during the recent epidemics How difficult it is to distinguish noninfluenzal from influenzal infections, grippe from la grippe, except during pandemics, is a matter of common experience Dr. Harry Jackson has told me that in patients dying of influenza at the Cook County Hospital enormous masses of mesenteric and retroperitoneal glands were frequent findings at necropsy.

The pathogenesis of such enlarged glands is again a matter of speculation. This is also true of the question that naturally arises whether they themselves cause the abdominal pain, assuming that they are related to it, or whether some antecedent inflammation of the intestine to which they are secondary, might cause it, or at least share in it. Two routes of infection are possible; by the blood stream and by direct transmission. The former seems improbable, for a marked general adenopathy is not especially characteristic of these infections. A selective localization is possible, as in many other infections, such as typhoid, and pneumonia, and epidemic meningitis. The frequently occurring cervical adenitis is not an analogous phenomenon, for here the invasion is manifest along the lymphatics and is strictly local.

A theory that they may be secondary to an invasion of the intestinal wall is certainly inviting though inconclusive. We are dealing with organisms that invade the mucus membrane of the throat, and other adjacent mucus membranes. It is at least possible that they have a similar action on the intestinal mucus membrane. They are undoubtedly swallowed in enormous numbers, and it is by no means proven that they cannot pass the stomach without losing their virulence. Even if the free hydrochloric acid of the stomach were germicidal enough to kill or weaken them at times, it would not be present free during the early part of the digestion of a meal during which time liquid contents are constantly leaving the stomach, carrying the organisms with them. We all know that in certain of these epidemics of throat infection, or grippe, indeed of influenza itself, what is apparently a true enteritis

is a frequent occurrence. That these are not digestive disturbances is evident from the fact that they are quite uninfluenced by dietetic treatment and last for some time. In these cases with abdominal pain, however, enteritis in the usual clinical sense, with diarrhea and nondigestion, is not a part of the clinical picture. Possibly, here only certain portions of the intestinal tract are invaded, as we know so well that different parts of the respiratory tract are involved at different times and in different individuals, and this may lead to localized inflammation without diarrhea but with attendant adenitis. The true cause of the pain may then, indeed, be, at least in part, a localized enteritis or colitis, rather than the lymphadenitis itself, and possibly some specific or selective localization may account for the fairly constant pain in the umbilical region. This might, perhaps, better than anything else, explain the varying nature of the pain, depending on the site and degree of involvement and on the amount of peristalsis that might be a factor in producing it.

That the glands might become involved secondarily, even to the point of abscess formation, or might continue to be enlarged for a time after the intestinal lesion is healed, is probable enough and exactly analogous to what happens in the secondary adenitis of the cervical and retropharyngeal lymph glands following a throat, or postnasal infection. Such glands could explain the recurrent pain in the abdomen that I saw in a boy aged 4 years for several months after a throat infection. Many times each day he would suddenly stop in his play and, saying "There it is again," would bend over as if he had a fleeting colicky pain. Pressure from gas, or some peculiar condition of peristalsis could easily elicit the pain at varying intervals. One wonders whether in such a case we do not overlap the condition of "umbilical colic" first described by Moro, and recently emphasized by Hutchison, in which there is such an intermittent colicky pain referred to the umbilicus and occurring over a period of months, especially after eating, when peristalsis would be most marked.

While our interest in the pathogenesis of this pain may be purely speculative, and while the pain may be of little intrinsic importance itself, it is of practical value from a diagnostic standpoint to know that there is such a pain and to be familiar with its clinical setting. In my own opinion I would rank it first, not in severity, nor in importance, but in frequency, among the abdominal pains that occur beyond the period of infancy that come up for differential diagnosis. As long as the pain remains at the umbilicus, or as long as it invades the three other quadrants of the belly it leaves us interested but cool; but when it occurs in the lower right quadrant the abdominal specter begins to stalk. It is then some comfort to know that in children this pain is much more frequent in this region than is that of appendicitis. It is

a still greater comfort when a pain with little tenderness or rigidity occurs in that fateful and uncertain region to find that the patient has a well marked throat infection, or what is of equal significance an otitis media, or a cervical adenitis, or a cough.

One must not, however, dwell in a fool's paradise when this condition arises. I well remember the case of a child aged 5 that had a definite throat infection and a slight pain and some tenderness over the region of the appendix. A surgeon of the first rank who saw the patient with me and who was quite familiar with the pain I have attempted to define thought that with such vague symptoms, in the presence of a throat infection, operation was not indicated. Two days later he changed his mind and removed a gangrenous appendix. Perhaps even here we can have recourse to the view of some of the older clinicians and of some French observers who believe, and I incline to share that belief, that among the complications that may occur with throat infections, or grippe, appendicitis itself must be included.

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SOME RECORDS REGARDING ABSENCES AND THEIR CAUSES IN THE LINCOLN SCHOOL OF TEACHERS COLLEGE

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As a part of the work of the office of school physician, a study has been made of absences and their causes. Additional data are needed and it is hoped that other schools will publish their data and methods of recording.

The need for several such studies will appear to anyone who considers the length of the school year and the amount of absence. In the public schools of New York City the number of school days in a year is about 190. In private schools the number is about 165 days in the higher grades and about 155 days in the lower grades. With such a short school year it becomes increasingly important that each pupil shall lose as few days as possible.

Health is now considered the most important element in education. Other factors being equal, the attendance record of a school is bound to reflect the health of the pupils. Furthermore, the keeping of a record of the cause of each absence brings to light the weaknesses of the individual pupils.

The records have been made in the following manner. There is in the physician's office a large chart on which the names of all the pupils are listed. Opposite each name is a series of small squares, each square representing one school day. If the child is in school, this square is left blank. When the child is absent, a dash is inserted in the appropriate square. When the child returns to school a check mark is inserted in the square representing the day on which he returns. Beneath these dashes is written the cause of absence, such as tonsillitis, cold, etc. The names of all the pupils in one grade are grouped together. Thus, it is a simple matter to tell how many pupils are out of school on any day and the causes. Absence records are turned in by each teacher at the end of the school day and recorded on the chart the following morning. The records of readmission are made by the physician when he passes the pupils. A pupil who has been absent for any cause has to report to the physician's office before reentering his room. The physician hears the child's story, makes what examination he considers necessary, and if the child is in condition to return to school, gives him a readmitting slip. This method has enabled us to keep out of the school rooms many children who were still in condition to spread disease.

No daily examination of the children in the class rooms has been made by the physician. If the teacher notices that any child appears

to be ill on entering school, he is immediately sent to the physician who examines him and sends him back to the class room or home, depending on what he finds. Many children who have been in school continuously but regarding whose health the parents are not certain are sent to the physician before going to the class room. In this way also a certain amount of disease is excluded which would otherwise not be discovered until more or less harm had been done. We feel that more and more children will be excluded as the cooperation between parents and the school authorities becomes more perfect. It is impossible to inspect every child each morning, nor do we think that much more would be accomplished if this were done.

The Lincoln School is a day school in New York City and is a part of Teachers College. The buildings occupied by the school are an old school building and a remodeled dwelling. They are far from perfect as regards space, light and air. The pupils attending the school come from all kinds of homes. As some of these homes are situated in the poorer parts of the city, it would seem that there would be more likelihood of these children bringing in infection than in those schools where all the pupils come from more carefully protected homes. The pupils are from 6 to 18 years of age, and about equally divided between the sexes.

In making up the statistics a child has been counted as a pupil until actually withdrawn from the school. This is contrary to the custom prevailing in most of our public schools where a pupil is considered as withdrawn after being absent three consecutive days. To illustrate, one boy was absent about three consecutive months last year. Every one of these days was counted an absence.

In the School year 1917-1918, there were 121 pupils in the school. Records were kept for only the last ninety-eight days of this year. During this year there were several small epidemics in the school, one each of measles, german measles, chickenpox and mumps. None of these spread to any considerable extent. The total number of cases of each of these diseases and the number of days of absence caused thereby are shown in Table 1.

TABLE 1.—RECORD OF SCHOOL EPIDEMICS DURING 1917-1918

	Cases	Days Lost
Measles	10	111
German measles	6	60
Chickenpox	7	105
Mumps	17	189

During the second year, 1918-1919, there were 182 pupils in the school. An epidemic of influenza occurred in New York City that year and fifty of our children had it, with a loss of 679 days. It also affects the records because in the early part of the year a good many

pupils were kept out of school for fear of their contracting the disease. All of these days were counted as absences against each pupil. There were no epidemics of any of the contagious diseases except chickenpox during the second year and of this there were fifty-five cases during the year, with a loss of 624 days.

There were 206 pupils in the school in the year 1919-1920. During this year there was another epidemic of influenza in New York. Twenty-six pupils had influenza and they lost 247 days. It seems probable, however, that a considerable number of the absences reported as due to respiratory diseases (colds, sore throats and bronchitis), were really due to mild influenza. The only contagious disease which reached epidemic proportions was whooping cough, of which there were thirteen cases, ten of these being in one grade. These thirteen children lost 398 days. There were three cases of chickenpox with a loss of twenty-eight days, five cases of measles with a loss of 105 days, one case of german measles with a loss of 11 days and five cases of mumps with a loss of 67 days.

During the year 1920-1921, there were 222 pupils in the school. There was only one case of influenza during the entire year. There were, however, the following cases of contagious disease:

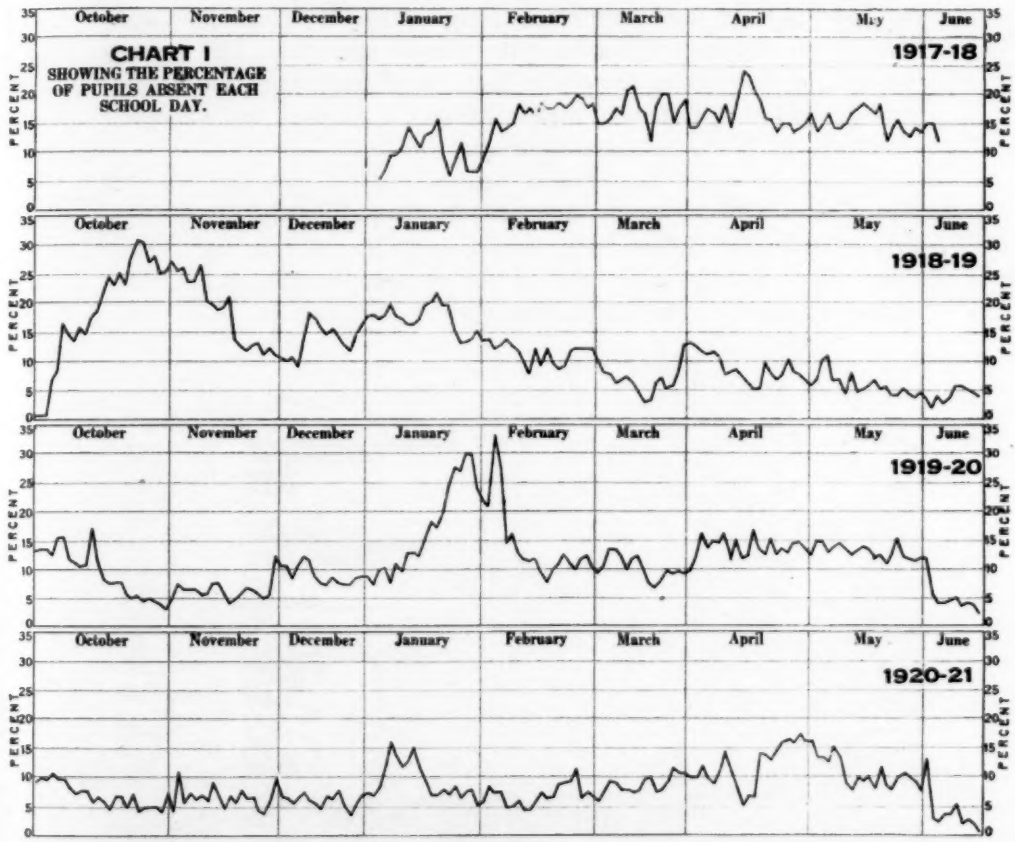
TABLE 2.—RECORD OF CONTAGIOUS DISEASES DURING 1920-1921

	Cases	Days Lost
Chickenpox	3	45
Measles	18	235
Exposed to measles and quarantined	4	35
Mumps	2	19
Pertussis	2	69
Exposed to pertussis and quarantined	1	10
Exposed to scarlet fever and quarantined	1	18

The only epidemic was one of measles, which occurred in the fourth grade. The trouble started from a pupil who stayed in school up to and including the day before the appearance of the eruption. He had not felt ill nor had his parents noticed anything wrong with him. There were twenty-three pupils in this grade at the time. Ten had had measles previously. These ten were not excluded from school and none of them developed measles. Every one of the thirteen nonimmune pupils developed measles. The original case was in school April 6, 7 and the morning of April 8. His eruption appeared April 9. The other twelve children who had not had measles, were left in school through April 15. After this they were excluded. Ten of them had been in school April 6, 7 and 8. Of these, three developed their eruptions April 19, two on April 20, four on April 21 and one on April 23. If we assume that the original case was contagious on the three days previous to the appearance of the eruption, and that the eruption appeared on the fourth day, the shortest possible period of incubation

was eight days and the longest fourteen days. One pupil was in school April 6 and the morning of April 7. This pupil's eruption did not appear until April 27, twenty days after her last exposure, making her incubation period at least seventeen and possibly eighteen days. We were unable to learn on which day the twelfth child's eruption appeared.

Two pupils in other grades developed measles about the same time. One, whose eruption appeared April 22, had walked to school with the original case on April 7. The incubation period was twelve days.



Another, a brother of one of the pupils in the fourth grade, developed measles, his rash appearing April 23, three days after his brother's rash appeared. Probably he was exposed to the original case but we were unable to find out when. Three of the second line cases had younger sisters in the school. Only one of these developed measles. Her rash appeared April 29. Her brother's rash appeared April 19 and she was last exposed to him April 15, making her incubation period eleven days. Thus the shortest possible incubation period was eight

days and the longest eighteen days. These incubation periods would indicate that it is perfectly safe to leave exposed children in school for seven days after their exposure, and that they may show the first symptoms of measles at any time during the next fourteen days.

The number of absences fluctuated markedly from day to day without any constant curve in all four years. The daily absence curves for the four years are given in Figure 1. As the total number of pupils varies from year to year this chart has been made up, not from the actual number of pupils absent, but from the percentage which this number is of the total number of pupils attending school that year. This makes the curves for the four years comparable. The average level of the curve falls steadily in each succeeding year. The marked increases in the early part of 1918-1919 and in January and February, 1920, are due to the influenza epidemics.

In Table 3 is given a detailed statement of the days lost from all causes. It is interesting to note that the largest groups in the first two years are the children who were not ill. In the third and fourth years the largest group is that of the respiratory diseases. Of the contagious diseases, chickenpox caused the most absences.

TABLE 3.—DAYS LOST WITH CAUSE

	1917-1918*	1918-1919	1919-1920	1920-1921
Chickenpox	105	624	28	45
Diabetes	...	...	44	48
Diphtheria	...	9	3	...
Eyes	...	17	37	30
Headache	...	...	...	17
Indigestion	...	79	225	257
Influenza	96	679	247	15
Malaria	...	...	5	...
Malnutrition	...	...	...	7
Measles	200	15	105	270
Measles (german)	60	...	11	...
Menses	...	...	22	19
Mumps	189	...	67	19
Not ill	717	1,134	512	506
Pertussis	97	...	398	79
Pneumonia	70	...	...	...
Poison ivy	...	...	...	18
Pyelitis	...	...	...	5
Respiratory	212	990	1,818	1,430
Rheumatism (acute articular)	...	...	91	...
Scarlet fever	...	...	17	18
Skin	...	52	...	1
Surgical conditions	28	52	96	155
Teeth	...	...	...	4
Typhoid	...	...	48	...
Vaccination	...	...	...	29

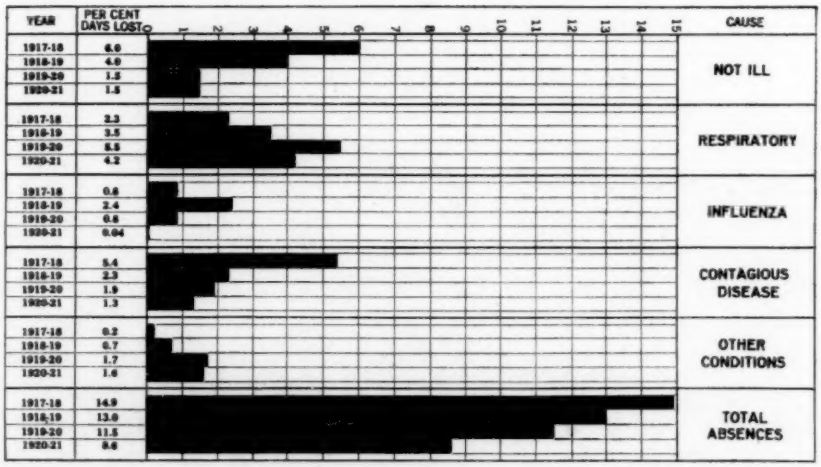
* Figures cover period from Christmas holidays to end of the school year.

In Table 4 and Figure 2 the absences have been collected into five large groups of related diseases and the percentages of days lost from each group worked out. The first group includes those absences that are not due to illness. A few of these are due to very bad weather but the majority are due to week ends in the country during the spring and fall and to staying away from school for one or two weeks at the

beginning and end of the school year. In 1917-1918, 6 per cent. of all days were lost due to this cause. The next year the percentage fell to 4 per cent. Even this meant that 1134 school days were lost, mostly for insufficient reasons. In 1919-1920 and in 1920-1921 only 1.5 per cent. of school days were lost due to this cause. This is a marked improvement and is entirely due to better cooperation on the part of parents. It seems as though this group of absences should be almost entirely eliminated. With this in view we have endeavored to make clear to the parents the importance of each school day to the child, and the added burden which week ends in the country place on the other days of the week.

TABLE 4.—Per Cent. of Days Lost and Cause Therefore

	1917-1918		1918-1919		1919-1920		1920-1921	
	Days Lost	Per Cent.	Days Lost	Per Cent.	Days Lost	Per Cent.	Days Lost	Per Cent.
Not ill	717	6.0	1,134	4.0	512	1.5	506	1.5
Respiratory	282	2.3	990	3.5	1,818	5.5	1,430	4.2
Influenza	96	0.8	679	2.4	247	0.8	15	0.04
Contagious Disease	651	5.4	648	2.3	629	1.9	431	1.3
Other conditions.	28	0.2	200	0.7	568	1.7	590	1.6
Total absences..	1,774	14.9	3,651	13.0	3,774	11.5	2,972	8.6
Possible total absences	11,858		27,990		32,572		34,189	



The group of absences due to influenza explains itself. During the fall of 1918 there was a severe epidemic of influenza in New York. Fifty pupils reported having the disease. They lost 679 days. As most of the cases occurred about the same time, the daily absences were very great for a short period. Yet only 2.4 per cent. of all the school days were lost due to this cause. In 1919-1920 there was another epidemic of influenza in New York, but few of the pupils reported having had

the disease, with a loss of only 0.8 per cent. of all school days. This figure is exactly the same as that for 1917-1918, the year before the large epidemic. During the year 1920-1921, there was only one case of influenza reported with a loss of fifteen school days which was equivalent to 0.04 per cent. of all school days.

The group of contagious diseases is extremely interesting. These are the diseases most feared by school authorities. In the year 1917-1918, they caused a loss of 5.4 per cent. of all school days; in 1918-1919 a loss of 2.3 per cent.; in 1919-1920 a loss of 1.9 per cent., and in 1920-1921 a loss of 1.3 per cent. of all school days. A detailed statement of the number of cases of each disease has been given already. The astonishing fact is the steady decrease in the percentage of school days lost due to this cause. This hardly seems due to chance. One is forced to believe that it is due to keeping track of the cause of absence of each pupil and having all pupils who have been ill, undergo medical examination before returning to their class rooms. On several occasions children who were unquestionably in condition to spread contagion have been kept out of school by this means. The important element would seem to be the having of a person on hand who is capable of deciding the question then and there and the freeing of the school from the necessity of accepting the decisions of parents and of doctors who may not have seen the child for several days.

During the four years, we have never closed a grade because of disease. This is contrary to the custom of many private schools. We have followed no absolute rules in regard to the exclusion of children who have been exposed to the different contagious diseases but have decided each case on its individual merits. Fortunately we have had no outbreak of scarlet fever or diphtheria. When a child has been definitely exposed to measles and has not had the disease, we have allowed the child to come to school for the first eight days after exposure. We have then excluded the child until about the sixteenth day. While the child is still coming to school he has seen the physician each morning before entering his room. A similar rule has been followed with chickenpox. Children with measles have been excluded from school for at least eight days after the appearance of the rash and until all catarrhal symptoms have disappeared. The board of health rule in New York excludes them for only five days after the appearance of the rash. Cases of chickenpox have been excluded until all scabs were off. Cases of mumps have been excluded until the second day after the complete disappearance of the swelling.

The group entitled "Other Conditions" includes accidents, surgical conditions and diseases which occur occasionally, such as diabetes, rheumatism, typhoid fever, etc. There will always be a small number

of absences due to these causes, none of which can be controlled by the school. The large number of days lost in 1919-1920 were mostly due to one case each of diabetes, acute inflammatory rheumatism and typhoid fever.

The remaining group is that of the respiratory diseases. Under this heading are included all infections of the respiratory system—colds, tonsillitis, laryngitis, otitis, bronchitis, and pneumonia. Influenza has been separated because of the large number of cases in 1918-1919. This is the one group which has not shown improvement. They caused a loss of 2.3 per cent. of all days in 1917-1918, of 3.5 per cent. in 1918-1919, of 5.5 per cent. in 1919-1920 and of 4.2 per cent. in 1920-1921. The high figures of 1919-1920 may very well be due to many mild cases of influenza being reported as colds, etc. The surprisingly low figures for influenza in that year would bear out this suggestion. In spite of allowing for some discrepancy due to this cause, the number of days lost from this cause increased steadily until the past year which shows a decrease of over 1 per cent. It is interesting to note here that Dr. Richard Smith [1] reports that this is the greatest cause of absence in an open air school near Boston. His figures are almost the same as ours for 1919-1920. It was our custom to exclude all children with colds from school for the first two days of the disease. This was apparently not sufficient. It is difficult to say just when it becomes probable that a child with a cold will not pass it on to other pupils. For the past year we have excluded all pupils with colds, etc., as long as they were sneezing or coughing or had any considerable nasal discharge. This kept each child, that became ill, out of school a day or two longer but the better figures for the past year would indicate that the number of cases was less and also the total number of days lost. This rule should be more rigidly enforced in the lower than in the upper grades because the pupils in the lower grades each have about twice as many colds as those in the upper grades.

In the group of Total Absences there is a steady improvement. In 1917-1918, 14 per cent. of all school days were lost; in 1918-1919, 13 per cent. were lost; in 1919-1920, 11.5 per cent. were lost and in 1920-1921 only 8.6 per cent. were lost. This is a definite improvement and means a saving of over two thousand school days in the last year. There is, however, still room for improvement particularly in the group of respiratory diseases.

1. Am. J. Dis. Child. **18**:246 (Sept.) 1919.

RARE CARDIAC ANOMALY

COR TRILOCULARE BIVENTRICULARE IN MIRROR-PICTURE DEXTROCARDIA WITH PERSISTENT OMPHALO-MESENTERIC BAY, RIGHT AORTIC ARCH AND PULMONARY ARTERY FORMING DESCENDING AORTA *

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In the remarkable case of congenital cardiac disease here recorded a complete absence of the interauricular septum is associated with other anomalies of a very unusual character, the whole forming a combination which, we believe, is unique in the literature.

CASE REPORT

Clinical Data.—A female infant, 17 days old, of Italian parentage was brought to the New York Nursery and Child's Hospital in a moribund state. The family history was negative. The child was of full term, normal delivery. Three days before admission the parents noted for the first time slight cyanosis of the extremities and somewhat difficult respiration.

On admission the infant presented extreme general cyanosis and Cheyne-Stokes' respiration. Both sclerae and conjunctivae contained extravasations, and several hemorrhagic spots were noted over the body. The apex beat was extremely faint—best heard to the right of the mid-clavicular line at about the sixth interspace. A faint prolonged systolic murmur was best heard at the base of the heart to the right of the sternum. The entire right thorax gave a flat note on percussion—no breath sounds were transmitted. The left thorax was dull on percussion—moist râles and harsh breathing were heard throughout. The heart outline could not be made out. The abdomen was distended and gave signs suggestive of fluid. There was a purulent discharge from the umbilicus. The liver was palpated below the umbilicus and the spleen 5 cm. below the ribs. The patient died two hours after admission. No blood culture was taken, and no thoracentesis was done.

Death was thought to be due to some form of congenital heart disease with cardiac failure, and also a possible septicemia and empyema.

Necropsy Summary.—At the necropsy the infection of the umbilicus was found to be superficial, and did not extend into the umbilical vein. There was marked engorgement of the abdominal contents and a small amount of free fluid in the peritoneal cavity. The liver, which was of normal size and markedly congested, was pushed down by a bulging right diaphragm. An interesting group of six supernumerary splenules were noted. Upon removal of the sternum, the pericardium was found to extend well out to the right, was greatly enlarged, and contained a moderate amount of transudate. The

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heart itself was tremendously enlarged and of a beef red color. The vessels and auricular portion were markedly distended with blood. The apex was broad and formed by both ventricles, giving the organ a globular shape. The right pleural cavity contained a large amount of transudal fluid—the left, a small amount. Both lungs were markedly engorged.

Description of the Heart.—Referring to Figure 1, it will be noted that there is a transposition of the ventricles and great vessels producing a "mirror picture" of these structures. The right chamber (left systemic ventricle) is somewhat smaller than the left chamber (right pulmonic ventricle), and on opening these chambers it was noted that the valve leading to the left chamber

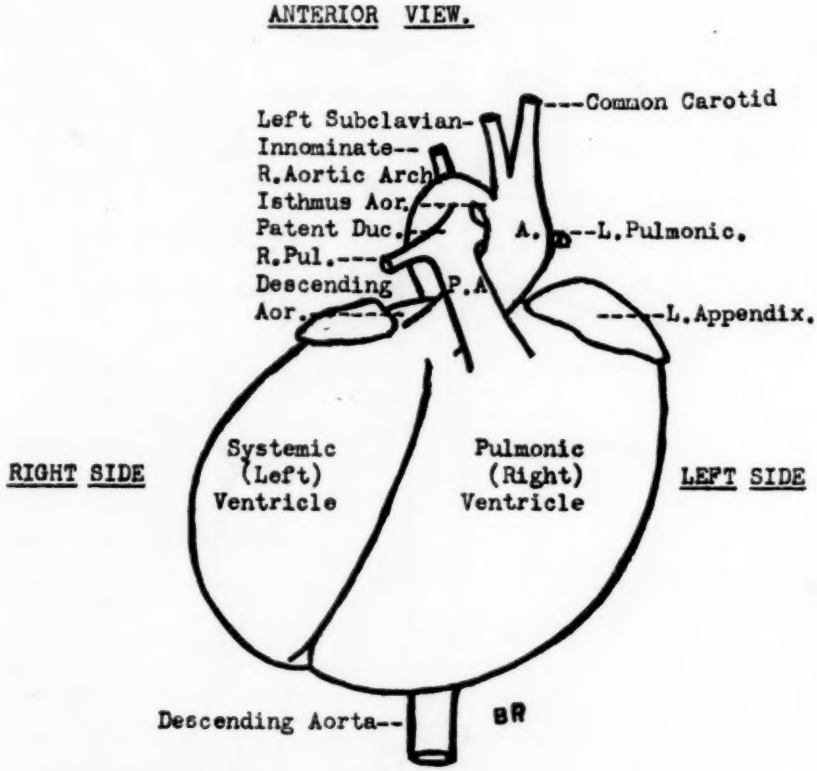

Figure 1

(pulmonary ventricle) was of tricuspid formation and the one leading to the right chamber (systemic ventricle) was of bicuspid formation. The ventricular septum is entire. The pulmonary artery arises from the anterior and right angle of the base of the pulmonic ventricle (left chamber) and runs upward and backward for about an inch to reach a plane posterior to the ascending aorta and terminates by dividing into three branches. A left and right pulmonary branch going to the hilum of each lung, the third branch, several millimeters long, a direct continuation of the parent stem, unites at an acute angle with what appears to be a corresponding branch from the ascending aorta. The latter is really the greatly narrowed continuation of the parent stem of the ascending aorta, the pulmonary artery forming the descending aorta through the greatly dilated ductus arteriosus.

The ascending aorta sprang from the base of the systemic ventricle (right chamber) and passed upward, forward and to the left. It extended for about one inch and also terminated by dividing into three branches, namely a left common carotid, a left subclavian, and a third short branch—a stenosis of the parent stem—which in common with the branch from the pulmonary artery described above (the dilated ductus arteriosus) gave rise to the descending aorta. These two anomalous short branches from the pulmonary artery and aorta were respectively found to be a patent ductus arteriosus and a stenosis of the isthmus aortae (Fig 1).

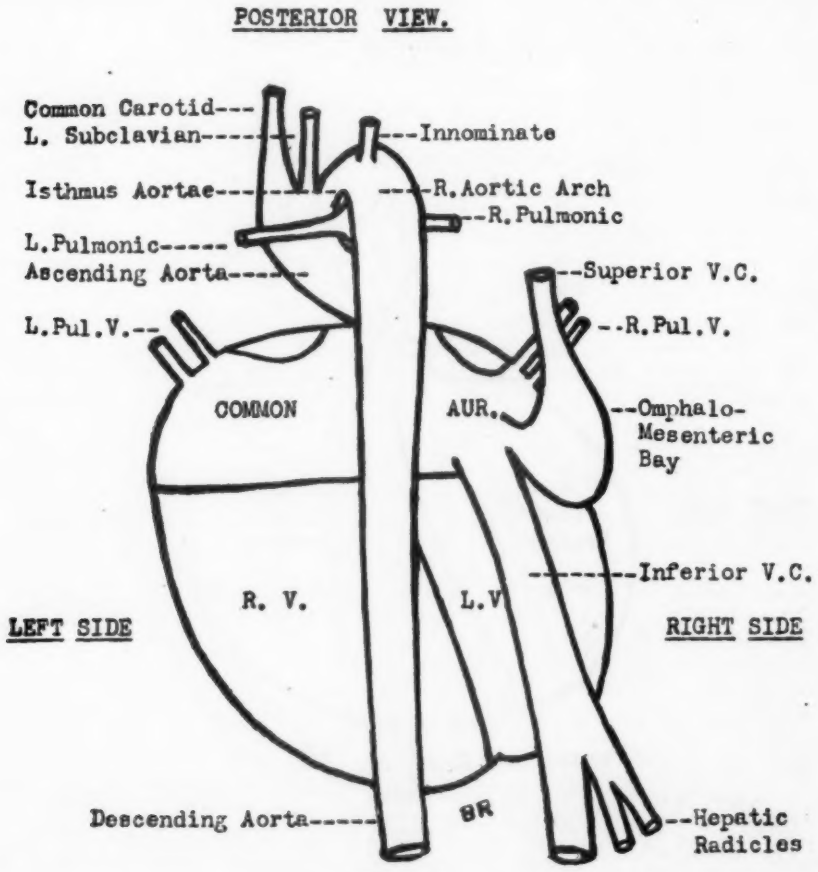

Figure 2

The descending aorta immediately turned backward to descend along the right side of the vertebral column (right aortic arch).

Viewing the heart from behind (Fig. 2) the innominate artery is seen to arise from the descending aorta near its origin. The presence of a right aortic arch and the narrowing of the aorta at the isthmus are here seen more clearly.

Examination of the auricle reveals several features of great interest and rarity: (a) There is no trace of the interauricular septum, the common auricle opening below into the two ventricles through the two transposed auriculo-ventricular orifices; (b) there are four pulmonary veins (Fig. 2) disposed in

pairs on either side of the median line in the roof of the auricle, those entering on the right side being in close juxtaposition to the mitral orifice which leads into the right chamber (L. V.) and thence into the aorta, and those on the left in similar relation to the tricuspid orifice which leads into the left chamber (R. V.) and thence into the pulmonary artery; (c) the superior vena cava (Fig. 2) descends from above in its usual course but is continuous before its entrance to the auricle with an ovoid pouch-like sinus which lies vertically along the right lateral wall of the auricle and enters this by a narrow mouth which transmits the blood from the superior cava, no other vessel entering the sac. As stated above, this is thought to be a persistence of the dilated right omphalo-mesenteric vein at its entrance to the right sinus horn, the vein itself having become obliterated in the next stage of embryonic life. The inferior cava enters the auricle from below by a broad orifice with distinct lips which lies in such close relation to the opening of the superior cava through the sinus above described that its upper border forms the lower boundary of the latter (persistent double sinus venosus). The position of these structures on the right side of the common auricle is evidence that this chamber is not transposed in spite of the transposition of the ventricles and right aortic arch.

The ventricular walls, papillary muscles, and chordae tendineae are greatly hypertrophied.

Summary of Anatomic Findings.—Mirror picture transposition of ventricles and great trunks (true dextrocardia) and right aortic arch. Auricles not transposed but lie in normal relation to the reversed ventricles.

Complete absence of interauricular septum (cor triloculare biventriculare) right pulmonary veins enter common auricle to right of median line. Superior vena cava entering persistent omphalo-mesenteric bay and inferior vena cava opening into auricle close to its mouth (double sinus venosus).

Ventricular septum entire. Patent ductus arteriosus and stenosis of the aorta at the isthmus, pulmonary artery forming descending aorta through greatly dilated patent ductus. Great hypertrophy of heart especially of pulmonic side. Multiple accessory spleens. Pleural effusion, great engorgement and passive congestion of viscera. Deep cyanosis (morbus caeruleus).

Diagnosis.—Beyond the existence of a dextrocardia it was, of course, impossible to distinguish during life the exact type of the complex cardiac anomaly here present, nor was a diagnosis attempted before death. The position, however, of the heart on the right side of the body without situs inversus of the remaining viscera pointed, as shown below, *to an arrest of development at that period of early embryonic life when the heart was still situate to the right of the median line,* before the speta had formed, such as might result in a biloculate or triloculate heart; and the marked cyanosis present would confirm this view.

The prolonged basal systolic murmur was undoubtedly due to the passage of the blood through the dilated ductus. A statistical study made by one of us (M.E.A.) has shown that the to and fro machinery murmur characteristic of patent ductus is a development of later life, and is not usually present at birth.

Pathologic Physiology.—Congenital cyanosis, or the symptom complex of deficient oxygenation of the blood through mechanical interference with the circulation by cardiac defects, may, as is well known, be produced by obstruction of the pulmonary circulation (by far the most serious cause and leading to the most extreme grades of cyanosis), or by mixture of venous with the arterial stream. In the present case, as intimated above, the latter cause was at work, for the pulmonary artery was widely dilated, and transmitted freely, both the blood to the lungs, as well as to the lower part of the body through the descend-

ing aorta, and the great hypertrophy of the pulmonic ("right") ventricle showed that these functions were being strenuously carried on.

The course of the blood may thus be traced briefly (Fig. 3): The blood from the superior and inferior cavae entering the right side of the common auricle meets the blood entering from the right and left pulmonary veins and passes synchronously through the transposed mitral and tricuspid orifices into the systemic and pulmonic ventricles whence it is distributed in a mixed stream to the head and upper extremities, a relatively small portion passing through the narrowed isthmus aortae to meet the current from the pulmonary artery to go

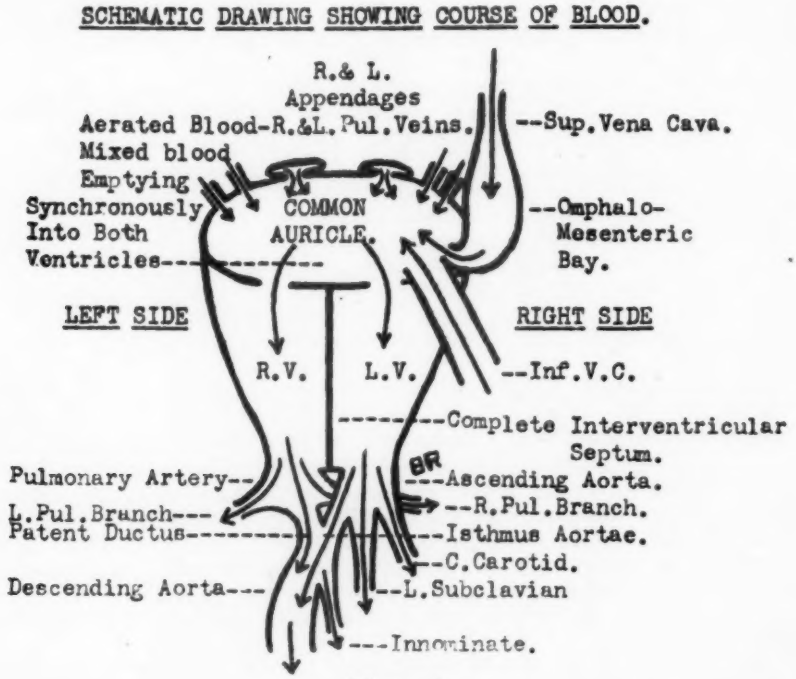

Figure 3

into the descending thoracic and abdominal aorta supplying the lower parts of the body.

It is thus readily seen that under the anatomic conditions that existed, if the ductus had become closed the amount of aerated blood in the systemic circulation would have been very small, for the venous stream entering the aorta is relieved only by the aerated blood from the right pulmonary veins, while that entering the pulmonic ventricle from the left pulmonary veins would have been returned to the lungs and there performed an almost useless cycle. It is clear that both the position of the right pulmonary veins just above the right auriculo-ventricular orifice, and the condition of the "pulmonary artery becomes descending aorta" were conservative adaptations whereby all the aerated

blood available was distributed respectively to the upper and the lower parts of the body through the two great channels thus made available.

DISCUSSION

The peculiarities of the case lie, first, in the very early stage at which arrest of development of the structures entering into the formation of the auricle and auricular septum took place, as evidenced by the primitive mode of entrance of the superior cava through what is undoubtedly, as was pointed out to us by Prof. G. S. Huntington, a persistence of the dilated terminal end of the right omphalo-mesenteric vein of the early vitelline circulation, and the situation of the entrance of this in close juxtaposition to the entrance of the inferior vena cava (persistent double sinus venosus?); and the displacement of the right pulmonary veins to the right of the common auricle. Secondly, the curious and bizarre character of the dextrocardia, in that, in the presence of a "mirror-picture" transposition of the ventricles and great arterial trunks the auricular part of the heart remained untransposed, the great systemic veins entering a "persistent omphalo-mesenteric bay" lying on the right side of the common auricle. We know of no set of conditions identical with these in the literature, although analogous observations have been published by Hickman,[1] Abbott,[2] and recently Keith,[3] in which transposition of the viscera (situs inversus) and of the auricles of the heart existed without transposition of the ventricles. The significant title "A Potentially Bicameral Heart" has been given by Dr. Keith to his recent very complete communication on this subject.

Other features, although by no means unique here, are the anomalous conditions of the systemic circulation, in that the main blood supply to the lower part of the body was transmitted to the descending aorta from the pulmonary artery through a greatly dilated ductus arteriosus. The main stream from the ascending aorta was directed through the great vessels of the neck to the upper part of the body, only a small portion passing through the stenosed isthmus to join the blood from the ductus arteriosus to enter the descending aorta. This condition of "pulmonary artery forming descending aorta" is usually compensatory in character, an adaptation to the needs of an obstructed or deoxygenated circulation from the left ventricle. Six such cases have been collected by one of us (M.E.A.) from the literature, and this is undoubtedly the explanation in the present instance. In a few rare instances the isthmus of the aorta is obliterated, or entirely absent, the ascending arch ending in the left subclavian while the pulmonary artery, dilated ductus, and descending aorta form a single large continuous

1. Hickman: Tr. Path. Soc. Lond. **20**:88, 1869.
2. Abbott, M. E.: Osler's Modern Medicine, **4**:345.
3. Keith: Case of Transposition of the Viscera Showing a Potentially Bicameral Heart, Proc. Roy. Soc. Med. Lond. **14**:3, 1921.

trunk; here a true anomaly existed due to the obliteration of the fourth, and the persistence of the fifth left primitive aortic arch. Such cases are reported by Hicks [4] and Barlow.[5]

The late appearance of the cyanosis, which was first noticed on the fourteenth day, and became very deep on the seventeenth (day of death) is usual in all except the most extreme grades of interference with aeration such as pulmonary atresia when morbus caeruleus is present at birth; and it is quite characteristic of the more moderate mechanical causes at work in the present case, in which there was no pulmonary obstruction, but only admixture of streams.

The Dextrocardia.—As has been pointed out by Kuchenmeister [6] and Nägeli [7] in their masterly monographs on this subject, congenital dextrocardia in which the heart lies to the right of the median line and the apex points to the right, is of two types; in the one, a mirror picture transposition of the heart exists in which all parts may be reversed and may bear their normal relations to each other. This condition does not necessarily constitute an anomaly, as in such cases the mirror picture transposition of the heart is nearly always associated with transposition of the viscera. In the other type of dextrocardia the heart is not reversed on itself, but remains in the right side of the thorax, through an arrest of development at this stage; here the chambers are not reversed on themselves, and grave anomalies are always present owing to the early period at which this arrest occurs. The two types of cases may be differentiated by the electrocardiogram, the mirror-picture type giving a reversal of the normal electrocardiogram while the second type shows the usual "right ventricular preponderance" of a severe congenital cardiac lesion.[8]

The present complicated case is of the mirror picture type, and the complete development of the ventricular septum suggests that normal (although transposed) conditions originally prevailed here. It seems possible that the hitch lay in the failure of the vitelline circulation to become duly obliterated so that the right horn of the sinus venosus became fixed in its attachment on the right side, and prevented or nullified the transposition of the auricular part of the heart, the other changes being secondary adaptations. In any case the combination of these two anomalies is suggestive and may possibly give a clue to the cause of situs inversus and the period when this occurs.

The Omphalo-mesenteric Bay and "Double Sinus Venosus."—The distinct pouch in which the superior vena cava ends was considered by

4. Hicks: Malformation of Aorta and Pulmonary Artery, Tr. Path. Soc. Lond. **15**:85, 1864.
5. Barlow: Congenital Heart Disease. Tr. Path. Soc. Lond. **27**:141, 1876.
6. Kuchenmeister: Leipzig, Thesis, 1883.
7. Nägeli: Deutsch. Arch. f. klin. Med. **96**:552, 1909.
8. Lewis: Clinical Electrocardiography, London, 1913.

us at first a persistent sinus venosus in spite of the fact that no other veins entered it with the superior cava. Our thanks are due to Prof. G. S. Huntington for kindly giving us the correct explanation [9] which is explained by Evans in his article there [9] in the following words: "The vitelline veins empty their blood directly into the liver sinusoids, the blood from the left omphalo-mesenteric vein being collected by a short trunk which enters the left horn of the sinus venosus (v. hep. sinistra); *but the right and larger one possesses a wide passage through this organ to the right horn of the sinus venosus.*"

A careful study was made by one of us (W.W.B.) of the comparative anatomy of the sinus venosus in relation to its opening into the auricle. The condition of double sinus venosus seen in Lepidosteus is simulated here, except that the coronary sinus did not open in connection with the other two veins. In Lepidosteus its homologue, the left ductus Cuvieri opens in common with the unpaired liver vein (inferior vena cava.) Rose.[10]

SUMMARY

1. Congenital dextrocardia is of two types due to (a) mirror-picture transposition (situs inversus) and (b) arrest of development. These types are of very different clinical manifestations and significance and may usually be readily distinguished.[11]

2. A case is recorded of complete absence of the interauricular septum (ventricular septum entire) in congenital dextrocardia of the mirror picture or situs inversus type in which the auricles have remained untransposed.

3. The absence of the auricular septum is associated with an anomalous entrance of the superior vena cava through a "persistent omphalomesenteric bay" which represents a structure persistent from the early vitalline circulation and which had probably been an etiologic factor in the lack of transposition of the auricles and possibly of the nondevelopment of the auricular septum.

4. The displacement to the right of the right pulmonary veins and the distribufion of the blood from the pulmonary ventricle to the descending aorta through the pulmonary artery are probably compensatory processes, to further the distribution of the available aerated blood to all parts of the organs and are not independent anomalies.

5. The cyanosis present is due to admixture of venous with arterial blood and not to pulmonary obstruction, and its late appearance here is explained on the ground of its more moderate character until compensation had failed and pulmonary congestion occurred.

9. Keibell and Mall, **2**:608 (Fig. 418) 1912.

10. Rose: Morpholog. Jahrb., 1903.

11. Meakins and Abbott: On the Differentiation of two Forms of Congenital Dextrocardia, Bull. Internat. Assn. Med. Museums, **5**: (June 1) 1915.

CLINICAL DEPARTMENT

A CASE OF TUBERCULOUS MENINGITIS WITH A DRY SPINAL SUBARACHNOID SPACE DUE TO DIFFUSE TUBERCLE INFILTRATION OF THE SPINAL MENINGES *

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The occurrence of a dry spinal subarachnoid space in tuberculous meningitis, due to a marked thickening of the spinal meninges from a diffuse infiltration with tubercles is a condition of great rarity.

In a study of 105 cases of tuberculous meningitis, recently reported by Meyers,[1] no mention is made of failure to obtain cerebrospinal fluid on lumbar puncture. The gross pathologic findings have been described in thirty-six cases of tuberculous meningitis by Espinet,[2] in nine cases by Rhein,[3] in thirty by Lutel [4] and Percheron,[5] without, however, any mention of such a marked diffuse infiltration of the spinal meninges with tubercles. Lesage,[6] Willerval,[7] Schoull,[8] Altman,[9] Neal,[10] and others, who have made special studies of the disease, do not mention this complication, nor do various standard textbooks make any reference to the condition. Leitch [11] has reported a case of tuberculous meningitis in which it was believed that the spinal subarachnoid space

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* From the Kingston Avenue Hospital, of the Bureau of Hospitals, Department of Health, New York City, Dr. Robert J. Wilson, Director, Dr. Wm. T. Cannon, Res. Physician.

1. Meyers, A. E.: Am. J. Dis. Child. **9**:427 (May) 1915.
2. Espinet, J.: Polynucleose rachidienne et meningite tuberculeuse, Paris Thesis, No. 28, p. 9, 1908.
3. Rhein, J. W.: J. A. M. A. **59**:165 (July 20) 1912.
4. Lutel, S.: Contribution a l'etude des formes anormales de la meningité tuberculeuse chez l'adulte, Paris Thesis No. 149, 1912-13.
5. Percheron, P.: Du diagnostic de la meningite tuberculouse chez l'enfant, Paris Thesis 1902-3.
6. Lesage, A.: La Meningite tuberculeuse de L'enfant, Paris, 1919.
7. Willerval, J. L.: La meningite tuberculeuse du nourrison, Paris Thesis, 1907-08.
8. Schoull, E.: Da la meningité tuberculeuse chez l'enfant, Paris, 1894.
9. Altman, D.: Les Hemorrhagies meningees au cours des meningities tuberculeuse, Paris Thesis, 1911-12.
10. Neal, J.: Tuberculous Meningities in Ticès Practice of Medicine, 1920, p. 241.
11. Leitch, D. B.: Am. J. Dis. Child. **13**:348 (May) 1918.

was shut off by adhesions in the upper cervical region, giving origin to a condition of xanthochromia of the spinal fluid, but as the spinal subarachnoid space was not examined at necropsy, it was questionable how extensive the process really was.

REPORT OF CASE

History.—(Case 2,002).—Patient, aged 5 months, was admitted to Kingston Avenue Hospital, Oct. 1, 1920.

Family History.—Negative for tuberculosis.

Previous History.—The infant was breast fed, rather weak, but had never been ill before.

Present Illness.—Four weeks before admission, the mother noticed that the baby's eyes started to discharge. This was followed by fever and propulsive vomiting which continued nearly every day, once or twice, during the first week of illness. During the second week, the vomiting disappeared but periods of constipation alternated with diarrhea. The vomiting reappeared a few days preceding admission. The temperature, from the onset, has been variable; it was high in the morning and low in the afternoon and, at times, reached 104 F. The baby's disposition has gradually changed; he became quite fretful and irritable. He would often awaken startled from his sleep and scream out. He has prespired profusely during the few days preceding entrance to the hospital. One convulsion occurred about September 26. It was tonic in type and involved the whole body. The patient remained quite bright until September 29, when he lapsed into a semistuporous condition, following a severe convulsion. His eyesight had apparently been good until this time.

Physical Examination.—The patient, a well nourished and developed male infant, was acutely ill. He was in a semistuporous state, out of which he could however, be aroused. There was a moderate degree of opisthotonos. The fontanel was bulging. The pupils were unequal, the right one slightly larger than the left; both react sluggishly to light. Left upper extremity is rigid and the fingers are flexed. The left lower extremity is also spastic, and the right upper extremity is flaccid. Patellar reflexes are exaggerated. There is no ankle clonus or Brudzinski. Kernig's sign is positive on the right side. There is hyperesthesia of mild degree. There is a complete loss of vision in both eyes. Heart is not enlarged; sounds at apex are of fair quality, but rate decreases markedly during periods of temporary apnea. Lungs are negative, except for some bronchial râles heard anteriorly and posteriorly. Breathing is of Cheyne-Stokes type. Abdomen is rigid, tympanitis, and no masses are palpable. During the course of the examination, the patient had three clonic convulsions involving the left upper portion of the body.

Clinical Course.—October 1: A lumbar puncture was performed on admission at the fourth lumbar space and 12 c.c. straw colored fluid were removed under normal pressure.

October 2: The baby's condition remained about the same. He had occasional clonic convulsions. He took nourishment well and was only slightly stuporous. Lumbar puncture was performed at 10 a. m., the needle being inserted at fourth, third, second and first of the lumbar spaces, 6 c.c. of fluid being obtained. By a second puncture at 9 p. m., at same level, only a few drops of spinal fluid were obtained at each level. The eleventh and twelfth thoracic spaces were then tried, but without success.

October 3: Baby's condition distinctly worse. Fontanel was bulging and convulsions of clonic type were very frequent. Rigidity of spine and limbs was more marked.

Owing to the failure of spinal punctures, it was decided to try the ventricular route. At 10 a. m. the left ventricle was punctured by the usual technic and 30 c.c. of clear fluid were obtained under marked pressure. The diagnosis of

tuberculous meningitis on admission having been placed in question by the dry subarachnoid space, 8 c c. of antimeningococcus serum were allowed to flow by gravity into the left ventricle.

October 4: Lumbar puncture at various levels was again tried, and although, as on previous days, the needle could be felt to enter the subarachnoid space, only a few drops of fluid were obtained. Then a ventricular puncture was resorted to and 30 c.c. of slightly straw colored fluid were removed under less pressure than on the previous day and 16 c.c. of antimeningococcus serum was injected by gravity.

October 6: Ventricular puncture, 28 c.c. transparent slightly straw colored fluid were withdrawn, and 18 c.c. of antimeningococcus serum injected. (When the needle was first introduced small drops of blood and a small clot issued from the needle. On introducing the needle about ¼ inch deeper, the fluid was slightly blood stained, but later became clear and colorless. It was thought then, that the choroid plexus had been wounded and this was corroborated later by postmortem evidence.)

From October 3 to the day he died, October 7, he became progressively worse. Gavage was required to give nutrition as he could not swallow well. Vomiting of projectile type occurred several times daily. The rigidity of the extremities increased and opisthotonos became more marked.

Clinical Pathologic Report.—Spinal fluid of October 1 and 2: Globulin, 4 +; Fehling's, negative; slight increase in cells; lymphocytes; no bacteria found on smear or culture. Ventricular fluid of October 4, globulin, negative; Fehling's 2 +, no bacteria on smear or cultures, slight increase in cells, lymphocytes.

Ventricular fluid October 6: Globulin, 2 +; Fehling's, no reduction; slight increase in cells; lymphocytes; no bacteria on smear or culture. Colloidal gold test of spinal fluid October 1, 0000142210.

Necropsy Report.—Thymus is normal. Lungs: The left lung shows, in large part, normal looking colored tissue, but here and there, in the upper and lower lobes, are areas of dark red color firm to pressure, nodular and varying in size. Sections of these areas show them to be sharply demarcated from the surrounding tissues, of a purplish red color, firm texture, with no evidence of caseation or pus formation. The right lung is of different appearance. It is darker throughout. The nodular areas are more numerous, of a purplish red color and a little depressed below the pleural surface. On the pleura of the lower lobe, there is a small area of ecchymoses, slightly elevated. The right upper lobe shows a few nodular areas which, on pressure, exude a firm plug of fibrinopurulent material. These areas do not correspond to the bronchi. On the pleura of the right lung, anteriorly and posteriorly, there are a number of minute, whitish gray bodies, elevated and firm, about 2 mm. in diameter, evidently tubercles. Section of the middle and lower lobes shows areas of fairly typical tubercle formation, scattered diffusely throughout the entire organ. The middle lobe has a small firm area, 1.5 c.m. in diameter, which on section shows numerous white spots, probably degenerated tubercles. At the bifurcation of the bronchi, there is a mass of enlarged lymph glands, some of which are caseous and contain pus.

Heart: Showed nothing unusual.

Liver: The liver is of normal size; superior and inferior surfaces show numerous tubercles, about 1.5 m.m. in diameter. Section of liver shows tubercles scattered throughout the liver tissue.

Spleen: Has a similar formation of tubercles on the capsule to those seen on the liver. On section, the tubercles are found more numerous and very prominent; the substace is intensely congested and of a blackish red color.

Kidneys and Suprarenals: No tubercles seen; organs are normal in gross appearance.

Spinal Cord: Examination of the spinal cord shows a rare condition. On opening the dura, it is found difficult to strip back the dura from the piarachnoid without including nerve tissue, owing to the adhesions between the two membranes. There is practically no subarachnoid space existent at most levels, the dura and pia arachnoid being in contact. In the entire subarachnoid space, there are only a few c.c. of fluid. The most striking thing is the appearance of the pia arachnoid membrane; it is no longer a thin transparent membrane but is opaque, grayish white in color and thickened (from 2 to 2.5 m.m. in diameter), and literally converted into a tuberculous granuloma, there being millions of pearl colored small tubercles scattered throughout. The tubercles are so numerous that they are semiconfluent, giving the membrane a peculiar rough, uneven granular appearance. The white matter is not of as firm a consistency as normal, but it does not appear to be involved by the process. The tubercles extend up to the medullary region and are very numerous along the lumbar nerve roots.

Brain: On the superior surface of the brain, there is a fairly marked congestion of the pia arachnoid. The pia mater is semiopaque and, here and there, there are small groups of tubercles, from three to four in number. At the base of the brain, from the olfactory nerve and the optic chiasm down to the pons and medulla, the pia is much thickened, of a greenish yellow color, opaque, studded with innumerable tubercles, many of which are undergoing degenerative changes which give the appearance of a plastic exudate, but firmer in character. On the tentorial surface of the temporal lobe, the pia also shows tubercles, some of which are quite large. At the junction of the two lateral lobes of the cerebellum, the pia presents the same appearance. In the cisterna magna, there is quite an accumulation of fluid slightly tinted with blood but not purulent. The third ventricle is definitely enlarged, as is the opening into either lateral ventricle. The lateral ventricles are much dilated and the fuorth ventricle moderately so. The choroid plexus of the lateral ventricles and the ependymal lining contain innumerable tubercles. At the anterior portion of the left ventricle, there are a few clots apparently originating from the choroid and choroid-like in structure but detached from the plexus. Section of the white and gray matter of the cerebrum and cerebellum shows no gross changes. The pia, along the point of origin of the seventh and eighth cranial nerves, shows numerous tubercles.

Microscopic Pathology.—(By Dr. James Denton, pathologist to Brooklyn Hospital.)

Lung: The sections of lung contain giant cell and reticulated tubercles, which have fused in places. Caseation is limited. Between the tubercles there are areas of gelatinous pneumonia in which the alveoli are filled with large mononuclear elements.

Liver: There is a limited dilatation of the sinuoids and mild fatty infiltration. Discrete tubercles containing giant cells are present.

Spleen: The venous sinuses are dilated and filled with blood. Numerous tubercles, some containing giant cells are present.

Suprarenals: Show no changes.

Choroid Plexus: The choroid contains numerous tubercles of reticulated and giant cell type. There is also a marked endothelial and lymphocyte reaction. The vessels show some endarteritis.

Nerve Trunks: Nerve trunks of several of cranial and spinal nerves show the presence of tubercles in the sheath of the nerve.

Spinal Cord: The coverings of the cord contain giant cell tubercles and hyperplastic tuberculous products over the whole surface.

Diagnosis.—Generalized tuberculosis and tuberculous meningitis, external and internal.

Bacteriological Diagnosis: Smears from the caseous bronchial lymph nodes showed acid-fast bacilli, typical of bacilli of tuberculosis.

SUMMARY

A case of tuberculous meningitis is reported which presents a rare pathologic condition of the spinal meninges causing a dry spinal subarachnoid space. This was due to the diffuse infiltration of the pia arachnoid membrane, from the cervical to the lumbar region, with innumerable tuberculous granulations producing marked thickening of the membrane, and causing adhesions between it and the dura, almost completely obliterating the spinal subarachnoid space except in the spinal cul de sac. No case reports of a similar nature have been found in the literature reviewed.

INTERMITTING FEVER IN A CHILD DUE TO MASTOIDITIS

DIAGNOSIS BY POSITIVE ROENTGEN-RAY FINDINGS*

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The following case is of interest, demonstrating the importance of considering the mastoid cells as a possible source of infection in cases of unexplained fever.

REPORT OF CASE

History.—M. P., male, 13 years old, was admitted to the A. Jacobi Division for Children of the Lenox Hill Hospital, March 5, 1921. Normal birth. Breast fed. Normal development. Pertussis five years ago; varicella one year later; measles at 10; pneumonia at 11, followed by a discharge from the right ear which lasted a few weeks. No family history of tuberculosis or lues.

Present Illness.—Eight weeks prior to admission the patient had a "cold." One week later he developed a cough, which was worse at night than during the day. This condition lasted a few weeks. Seven weeks ago he complained of earache which was not very severe. Ten days later there was a discharge from the right ear which stopped after a few weeks. The patient has complained of weakness and loss of appetite. He has been constipated. At times there was severe frontal headache. About ten days before admission he developed another "cold," following which there was a definite chill every two or three days with high fever at irregular intervals. The patient has lost considerable weight.

Examination.—The examination on admission to the hospital showed a fairly well developed child whose general condition was poor. Weight was 53½ pounds. The skin and mucous membranes were slightly anemic. There was present a general moderate glandular enlargement. The left ear was negative. The right ear showed a very small perforation of the drum membrane from which there was no discharge. In all other respects examination of the ear was negative. There was no mastoid tenderness, nor any localized areas of tenderness about the head. The nose and throat were negative. The teeth were in fair condition. The tonsils had been removed. The lungs were negative. The heart showed a slight impurity of the first sound. The abdomen was negative. The reflexes were normal. The v. Pirquet reaction was positive. Roentgen-ray examination of the chest showed no evidence of tuberculosis. The Wassermann reaction of the blood and spinal fluid was negative. The fixation test of the blood for tuberculosis was negative. The blood culture was negative, as was also a chemical and bacteriologic examination of the spinal fluid. The urine did not show any abnormalities. No parasites or ova were found in the feces. In short, physical and laboratory examinations were entirely negative.

On admission to the hospital the temperature (Fig. 1) was 100.2 F. This gradually rose to 103 F. on the fourth day, dropped by lysis, and rose to 104 F. on the seventh day. It became normal for one day, and then rose to 104.4 F., dropping to normal by crisis. Two weeks after admission the temperature rose

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*From the A. Jacobi Division for Children of the Lenox Hill Hospital.

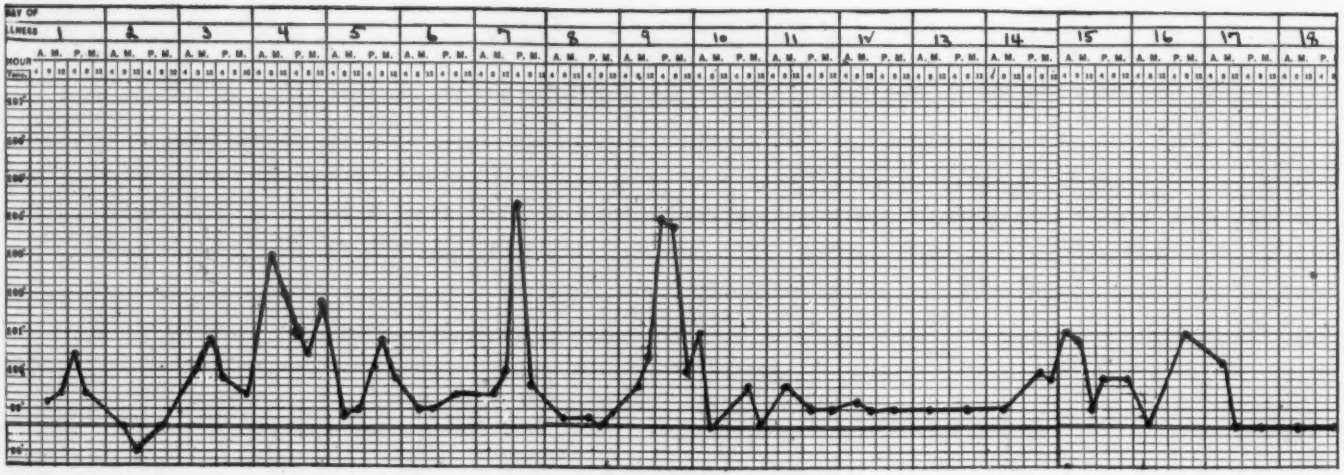

Fig. 1.—Record of temperature.

to 101 F., but dropped to normal within forty-eight hours, and was not elevated again during the ensuing three weeks observation in the hospital.

The patient had no chill while in the hospital. The pulse rate and respiration varied with the temperature as follows: pulse rate, from 80 to 120 per minute; respiration rate, from 18 to 32 per minute.

The blood examination on admission was: white blood cells, 12,000; polymorphonuclears, 70 per cent.; lymphocytes, 30 per cent. Repeated examinations showed no variation of this picture. Frequent examinations of the blood for malarial organisms were negative. The Widal reaction was negative.

The point of interest in this case was the intermitting fever. The physical examination, as the report shows, was entirely negative. All the laboratory tests were negative, with the possible exception of the white blood count which showed a slight leukocytosis. As a possible cause of the fever, influenza, pneumonia, tuberculosis, pyelocystitis, otitis media, malaria, typhoid fever, syphilis and nutritional disturbances were considered. After careful study all these conditions were ruled out.

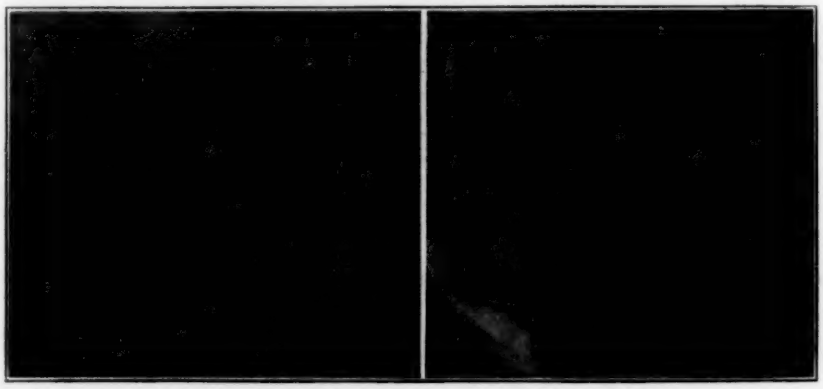

Fig. 2.—*A*, shows evidence of mastoiditis. Cells filled with exudate. *B*, shows normal mastoid cells (left side).

It then seemed advisable in view of the patient's past history of an ear infection and the presence of a perforation of the drum to have an roentgen-ray examination made of the mastoid cells, although there were no symptoms pointing to a pathologic condition of the mastoid. Roentgen-ray examination by Dr. W. H. Stewart (Fig. 2), made ten days after admission to the hospital, showed definite evidence of a right mastoiditis. The mastoid cells were filled with exudate so that the normal air spaces could not be distinguished. There was no evidence of necrosis.

During this time the patient's general condition had improved, the temperature remained normal or nearly normal, and there were no manifestations pointing to the ear. At the daily consultations with the otologist of the hospital (Dr. H. A. Ehrmann), it was decided that

inasmuch as the patient had gradually improved under expectant treatment, operative interference was not indicated. A second roentgen-ray examination (Fig. 3), made about one week after the first showed a partial absorption of the exudate. "The cell structure had become more distinct and the shadows were much clearer in detail. This would indicate some resolution. There was no evidence of advancement or breaking down." Further roentgen-ray examination two weeks later showed that the exudate in the mastoid cells was gradually disappearing. The patient's condition had improved remarkably, and he had gained ten pounds during the five weeks that he remained at the hospital. The last roentgen-ray examination, made about two months later, showed considerable improvement. There appeared to be an early sclerosis of the mastoid cells.

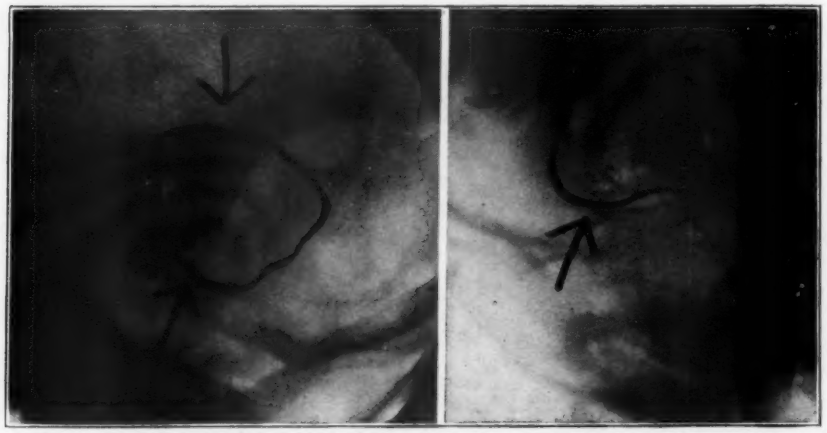

Fig. 3.—Taken one week later than Figure 2. *A*, shows clearing of exudate in mastoid cells, compare with Figure 2. *B*, shows normal mastoid cells (left side).

The roentgen-ray examination established the diagnosis of an obscure fever in this case, and, had it not been carried out the patient would undoubtedly have passed from observation with the diagnosis of "fever of unknown origin."